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# The Journal of the American Pharmaceutical Association

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Volume III JUNE, 1914 No. 6

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## DR. BEAL'S RESIGNATION.

THE members of the Association, without exception, will most gladly receive the news that the resignation of Dr. Beal, as Editor of the Journal and General Secretary of the Association, has not been accepted by the Council to take immediate effect, but that action upon that matter has been practically deferred until the convention in August, at which time every friend of the A. Ph. A., and of American pharmacy, will hopefully wish that Dr. Beal's health will have been so restored that he may be able again to resume the position which he has so signally honored.

In making this statement, I beg to be pardoned for intruding a personal acknowledgment of my most heartfelt regard and esteem for my chief, Dr. Beal, and to express my most sincere thanks to him, for the kindness and courtesy with which he received me as his assistant, and to say, that nothing could give me more satisfaction than to see him fully restored to health and once more occupying the desk and place he has made for himself.

In my occupancy of the position of Acting Secretary of the Association and Acting Editor of the Journal, I earnestly solicit from the members their sympathetic consideration. That I cannot fully fill the place of Dr. Beal, it is unnecessary for me to avow, but to him who has reposed this confidence in my ability, in selecting me as the temporary occupant of his place, and to every member of the Association, from the highest to the lowest, I pledge my most earnest effort to warrant his and their confidence and esteem. Should I fail in this endeavor it will not be from lack of desire to serve the Association to the utmost extent of my humble ability, to which effort I pledge my whole heart and soul.

ERNEST C. MARSHALL,
Acting Editor and Acting General Secretary.

## ASSOCIATION MEETINGS.

DURING the months of June and July many meetings of State Associations occur, and the pharmacists of the country will gather together in state conventions to consult and to deliberate as to the manner by which the interests of the profession,—and consequently their own most important interests,—can be advanced.

At these annual gatherings "many men of many minds" will convene and it is greatly to be desired that from their deliberations will come great and lasting good to the whole profession.

The members of our craft,—more than those of any other,—need the broadening influence which comes from association-work; the touching of elbows with other men of their profession; from the exchange of views with their fellows; from the tolerant listening to, and the weighing of other men's opinions.

It is not the relinquishment of our own ideas to respectfully hear and to carefully weigh the arguments which another brain has wrought out. In this great land of ours, where education is so universally diffused, the man from the back-country, in a small store, has perhaps used his gray matter to good advantage and, from his thought, may have evolved ideas productive of much good, if adopted. Nothing advances the interests of any organization more than toleration of other's opinions, and a desire to profit by the best thoughts of every one of its members, and we should, in all of these conventions, patiently listen to, and sift these thoughts carefully, in order that no wheat be thrown away with chaff,—nothing wasted that should be preserved.

The officers of all these associations have earnestly worked to promote the interests of the Association and the profession during the past year. They have kept a vigilant eye upon all legislation and have guarded against unwise attempts to fetter and to curb the general and natural advancement of the trade. To them should be accorded an unqualified support and an earnest loyalty. They have not worked for self-aggrandizement, but for the good of all. Let us then go to our State Conventions with an earnest purpose to support loyally all the efforts these officers have made in the interests of our craft. Let us listen thoughtfully and weigh well, all that is said at these meetings upon every question which is presented, and let us dedicate this period to the uplift and the advancement of the profession to which we look for our welfare and support. Not alone to play and to pleasure should these gatherings be devoted, but our Association meetings should mean work for every one, and let us from this work derive an enthusiasm, a loyalty, not alone to our state organizations, but to the great national organizations which make the profession of pharmacy a power in the nation. From this inspiration maybe will come a desire to go to Detroit to participate in the great national convention of the American Pharmaceutical Association from whose annual gatherings no one ever returned without being a better, a broader and a wiser man. What glorious results might follow if every pharmacist in the country came to the Detroit meeting and aligned himself and his influence in support of the policies, the achievements and the traditions of the A. Ph. A., and, returning home, would labor earnestly in his field of influence to advance the true interests of pharmacy, along the broad lines laid down by

Squibb, Maisch, Procter and the many others who labored so long and earnestly to make pharmacy a true and an honored profession,—one ranking with any other in the world. It is not necessary that members should devote their valuable time to work for the Association; to sacrifice anything. It only calls for them to hold it in their heart of hearts as *the* Association of the country and the world, the one which has ever held its rudder true to the highest ideals of pharmacy; to look up to it as their *Alma Mater,*—their loving mother,—whose ever-watchful care is over and around them, ever seeking for their weal.

In this spirit the old-time men of our craft served their guild, and made it their protection against the tyranny of the over-lords and others who would oppress them. To-day the Pharmaceutical Guild of the Nation,—the American Pharmaceutical Association,—has taken the place of the guild of the old burgs, for, under modern conditions, the men of Boston know the men of San Francisco as well as the men of olden time knew their *confreres* of the next city, and this intimate connection should make for a solidarity, a harmony and a strength which should be irresistible for good if properly utilized and fostered and it is by association-work that such results may be achieved.

If every member would grapple this thought to his soul and take this interest in the Association, much good would result to American pharmacy and every one of its members would attain to a higher, better and a more profitable position in the community.

DETROIT,—THE BEAUTIFUL.

Anyone who has visited Detroit can readily answer the question—"Why is Detroit the greatest convention city in the world?" Space precludes our giving the thousand and one reasons here. Suffice it to say that Detroit fully lives up to the reputation expressed in its world-wide known slogan,

*"In Detroit Life's Worth Living Every Day!"*

By virtue of its location, Detroit is preëminently the Convention City of America. Situated on the high terraced bank of its beautiful river,—the noble strait which connects Lake St. Clair and Lake Erie,—its climate is ideal for mid-summer gatherings. Its many beautiful public buildings, churches and other edifices delight the artistic eye, while a lover of Nature finds keen pleasure in the enjoyment of its magnificent parks, its boulevards and suburban drives.

Detroit will be the Mecça for many conventions this coming summer. The greatest of these will be that of the American Pharmaceutical Association which will be held August 24-29. An efficient entertainment committee has arranged a splendid program for your pleasure and benefit,—they say "There never was a better one." For this week Detroit will be the drug-center of the world where the great men of the profession will gather and confer as to the welfare of our noble craft. Your presence will add to the success of the convention, and you will have "the time of your life."

Send your notice at once to the Local Secretary, Mr. Leonard A. Seltzer,—tell him you will be in Detroit with us, and "be a Booster"; get your fellow-pharmacists to come along, and with them get away from the daily grind and broaden your horizon. You can greatly serve your Committee on Accommodations by sending your notice to-day. And you will also be assured of better quarters and service. You are confidently expected and will be cordially welcomed by your brothers of Detroit. Omar Khayyam sings:

"When all the temple is prepared within,
Why waits the drowsy worshipper without?"

Why then wait? Say to yourself, "I'll be in Detroit in August," and BE THERE.

THE DETROIT HOTELS.

Members of the American Pharmaceutical Association, expecting to attend the Detroit meeting, beginning Monday, August 24, will be interested to know about the various hotels and their rates. May we suggest, too, that reservations be made reasonably early in order to avoid any doubt about getting satisfactory accommodations? Detroit is well filled with tourists in July and August, and it would be most unwise not to reserve your rooms and thus make sure of getting them.

The hotels are as follows:

Pontchartrain (official headquarters)—$2 to $2.50 for single room, $3 to $4 for double room; $3, $3.50, $4, $5 for single room with bath; $5, $6, $8 for double room with bath.

Cadillac (one block away)—$2 to $5; rooms with bath 50 cents extra; $1 less than twice the price when two occupy a room.

Griswold (two blocks away)—$1.50, $2, $2.50, $3; $2 and upward for rooms with bath; add $1 to the price when two occupy a room.

Ste. Claire (American plan—two blocks away)—$2.50 to $4.50; $3.50, $4 and $4.50 with bath.

Tuller (four blocks away)—$1.50 and upwards; add $1.50 when two occupy a room.

Charlevoix (five blocks away)—$1.50 and upwards; add $1 to price when two occupy a room.

Wayne (eight blocks away)—$2, $2.50, $3, $3.50, $4; $3.50 and upwards for rooms with bath; $1 additional when two occupy a room.

Plaza (five blocks away)—$2 for single rooms; $3 for double rooms; meals 50 cents each.

Lenox (five blocks away)—$1 single room; $1.50 double room; $9 per week single room with bath; $12 per week double room with bath.

Addison (eight blocks away)—$2 and $2.50 for one room; $3 and $3.50 for two rooms; $4 and $5 for three rooms.

It will be observed that the only American hotel in the list is the Ste. Claire.

## EXCURSION FROM DETROIT TO PT. COCKBURN AND RETURN.

The trip from Detroit to Toronto is made in the elegantly appointed trains of the C. P. R. Leaving Fort St. Union Depot, the train soon passes upon the railway ferry, to be transferred to Windsor in Canada. From the middle of the stream, an excellent view of Detroit may be observed. Leaving Windsor, the train passes through a rich farming country to Chatham, London, Woodstock, Galt, Milton and Erindale, all prosperous manufacturing and farming communities. At Cooksville, Dixie, Summerville and Islington many Toronto people have their summer homes. At West Toronto, those tourists who do not care to visit Toronto, can make connection for Bala. Toronto is, however, most inter-

Shooting the Rapids — Muskoka Lakes.

esting, and well repays a visit to Canada's "Queen City." From Toronto to Bala are many beautiful views, among them being the Falls of the Severn and Muskoka. Leaving Bala, the tourist passes through the beautiful lakes of Muskoka, Rosseau and Joseph, which are situated some hundred and twenty miles from Toronto, and on the east of the Canadian Pacific line. Stretching fifty miles further north, is the famous Georgian Bay country. These two districts, comprising as they do rivers, lakes, islands and bays innumerable, form one of the greatest vacation lands yet discovered. This romantic network, of open lakes and intricate waterways, every year rings with the laughter of the city dweller, who finds in the clear waters and pine-clad islands of the Muskokas, in the sheltered inlets of Georgian Bay and Point Au Baril, and on the rocky shores of the French River that outdoor life which fills the lungs with purest of ozone, the body with new vigor, and the heart with new happiness.

"Own your own island," say some, and surely there is a wide choice, for there are thirty thousand islands in Georgian Bay. Those of more moderate desires

Canoe Sailing on Georgian Bay.

can, for a dollar a day, in some lake hotel or boarding house, breathe in the balsamic odors of pine and spruce, and with the daily swim, happy picnics and canoe parties, find exquisite enjoyment and regain health and joy of life.

Then there are those who scorn dwellings, and prefer camp-life in the open, taking with them bacon, flour, butter, sugar, salt and tea, needing but a fish or two from the cool waters to complete all that an epicure could crave.

By Canadian Pacific train from Toronto to Bala, the gateway of the Muskoka district, is some four hours' ride through a rich agricultural section, and a good service, combined with the fact that there are both United States and Canadian customs officers located at Bala station, makes the rail-journey unusually free from care and trouble. At Bala, transfer is made from train to steamer, and close connections insure quick arrival at any point on the lakes.

The principal lakes are three in number, Muskoka being the largest, Joseph next in size, and Lake Rosseau the smallest. They contain between four and five hundred islands, ranging from one of over 1999 acres, to those containing but a single tree or a rugged mass of rock. The majority, however, are densely crowded with pine, balsam, cedar, birch, maple, oak and other varieties of tree life.

These attractive lakes, however, do not monopolize the attention of the vacation seeker, for there are many rivers in this lovely region which offer an almost endless variety of canoe and motor-boating trips. Lake Muskoka itself is twenty-one miles long, and being joined with the other lakes by channels, a month could be easily spent in exploring their inlets, bays and rivers. Water sports are very popular in the Muskoka

Camping on Georgian Bay.

Regatta — Lake Rosseau — Muskoka Lakes.

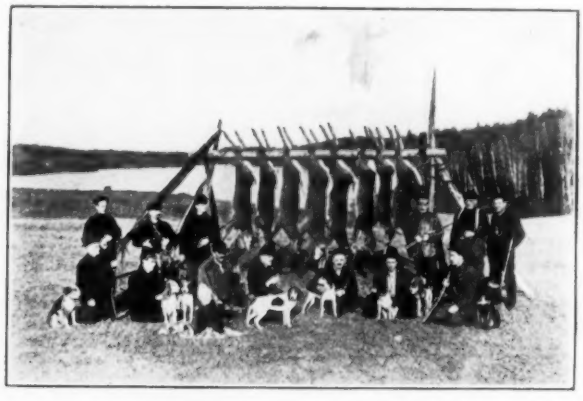
Lakes, regattas being a weekly occurrence, and often parties located at one end of the lakes will boat to a neighboring regatta, and enjoy the sport always to be found at these gatherings. At the many hotels and boarding-houses on the lakes will be found good tennis courts, bowling greens and golf links, where these pastimes may be enjoyed.

In the Georgian Bay District, where everybody lives on islands, yachting is one of the great attractions, and canoeing is safely enjoyed among the many passages. There is splendid fishing among the islands, bass being very plentiful. Parry Sound is a favorite point, but a little further north, at Point Au Baril, will be found a vacation-land which all will depart from with regret and a longing to return.

Its natural attractions are very wonderful, in fact the hundreds of islands appear to have been designed to supply the need of saluburious resorts, where, in the summer, people might go and forget business cares and be happy in a land of

Victorious Crew in War Canoe Race — Muskoka Lakes.

enchantment. The fishing is exceptionally good, black bass, pickerel, pike and muskalonge being found in abundance. In this region and the French and Pickerel River Districts, those who prefer camping-out, to hotel life, will find splendid facilities, as there are people who make a specialty of fitting up tents



A Day's Record near Parry Sound.

and camping outfits for parties. During the open season the inducements to the hunter are very strong, as the section within an eight-mile radius of Point Au Baril is one of the richest game lands in the country.

The canoe trips are innumerable, and a party can set out and, with portages, return, without having traversed the same waters twice.

The whole country between the Muskoka Lakes and Sudbury is a natural heritage which is becoming more popular yearly, as vacationists return from a happy visit bringing with them stories of the joys to be found among its waters and its woods.

# Book Reviews

BIOCHEMIC DRUG ASSAY METHODS WITH SPECIAL REFERENCE TO THE PHARMACODYNAMIC STANDARDIZATION OF DRUGS. By Paul S. Pittenger, Ph. G., Ph. C., Phar. D., Instructor of Pharmacodynamics, Departments of Pharmacy and Chemistry, Medico-Chirurgical College, Philadelphia; Member of Committee on Physiological Testing of the American Pharmaceutical Association, Member of the American Chemical Society, American Pharmaceutical Association, etc., Philadelphia; P. Blakiston's Son & Co.

This manual has been prepared for the use of students of pharmacy, pharmaceutic chemistry and medicine, and pharmacologic experts. It represents a very large amount of original work, and is especially valuable for teaching purposes. The illustrations, many of which are original, are exceptionally good.

The subject matter embraces preliminary considerations, cardiac stimulants and depressants, epinephrine and products of the suprarenal gland, ergot, pituitary extracts, cannabis indica, technique and apparatus and solutions employed.

The manual is an admirable exposition upon a branch of work that has become of the greatest importance in pharmacy—pharmacologic standardization,—and the author deserves to be congratulated upon it.

The importance of pharmacologic standardization does not need to be discussed before pharmacists, for most of them are well aware that this is the only way that reliable preparations of certain important drugs can be made. Some unthinking individuals try to minimize the importance of such procedure on the ground of anti-vivisection. Physiologic standardization is the only means of eliminating worthless preparations of a certain class from the market, and it is certain that where human lives are at stake, the sacrifice of a few animals under anesthesia cannot be condemned.

The title of the book, "Biochemic Drug Assay Methods," is open to criticism, because the book is really not a work on biochemistry, but on the pharmacologic standardization of drugs; and the definition given of pharmacology (p. 3) is open to serious criticism because it is obsolete.

The term pharmacology is derived from the two Greek words meaning "medicine" and "discourse," and as formerly used meant "the sum of knowledge regarding medicines." But times change and the meanings of words change with them. "Pharmacology, in the modern and accepted meaning, treats of the action of chemical substances on living tissue—of the changes produced in the structure, composition and function of living bodies by unorganized chemically acting substances not belonging to their natural environment. Pharmacology, therefore, goes a step further than what used to be called physiologic action, in that it aims to furnish the explanation for the changes observed." (Sollmann).

That this definition is the accepted definition of the medical profession of this country to-day is shown by the fact that the American Medical Association uses the title "Section of Pharmacology and Therapeutics" for its section devoted to the study of the action of drugs on tissues, and therapeutics.

W. A. PEARSON.

TREATISE ON GENERAL AND INDUSTRIAL ORGANIC CHEMISTRY. By Ettore Molinari, Professor of the Luigi Bocconi Commercial University, Milan. Translated from the second Italian edition by Thomas H. Pope, University of Birmingham. Cloth, 770 + xix pages, 506 illustrations. P. Blakiston's Son & Co., Philadelphia, 1913; $6.00 net.

This new book is a descriptive organic chemistry, written from the standpoint of the technical chemist, and combining descriptions of the organic compounds themselves with the technical applications of each group.

The author's idea is well expressed in the following quotation from the preface: "It does not suffice that the young chemist, about to begin his industrial or teaching career, should have a thorough knowledge, for instance, of the various syntheses and constitutional formulæ of the sugars. He should also be acquainted with at least the general outlines of the industrial processes and *technique* of the manufacture of sugar, beginning with the slicing of the beets and proceeding to the refining and centrifugation of sugar crystals."

The three divisions of the book are General, Derivatives of Methane, and Cyclic Compounds. Part I discusses the purification and analysis of organic compounds and the general theoretical discussions of organic chemistry.

The principal groups discussed in Part II are the hydrocarbons, alcohols, and derivatives, acids and derivatives, carbohydrates; and in Part III hydrocarbons and their immediate oxygen and nitrogen derivatives, aromatic acids, hydrogenated benzene nuclei, condensed nuclei, heterocyclic compounds, coloring agents and fabrics, proteins, glucosides, and other compounds of uncertain composition.

One thing which will detract from the value of the book to the chemist of America is the fact that methods described, costs quoted, and dimensions given are all or nearly all in terms in vogue in Europe. This is largely excusable in a translation when we think of the secrecy which surrounds so many of our present day works, particularly in this country.

Most industrial chemistries are interesting reading, and this book is no exception. Some particularly interesting descriptions are included, among which might be mentioned explosives, the fermentation industries, sugars, and fabrics. The book will find a place in many libraries and should be read with interest by both the theoretical and the practical chemists, and particularly by the young man just out of college, who is just beginning to realize the necessity for correlating his theoretical and practical training. GEO. D. BEAL.

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ANNUAL REPORTS OF THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION. Vol. VI, Jan.-Dec., 1913. Price 25 cents.

This publication should be in the hands of every pharmacist. It contains data of particular interest to them in regard to the various nostrums which have been discussed in the pages of the Journal of the A. M. A. during the past year. Familiarity with the facts therein stated should be effective evidence to convert many misled physicians from the prescribing of nostrums to the use of official preparations. As the methods of analysis used in the examination of these preparations are stated in detail, the manual is of much value to all druggists and others who are interested in the chemical examination of drugs and chemicals.

# Scientific Section

Papers Presented at the Sixty-First Annual Convention

## THE EFFECT OF GEOGRAPHICAL SOURCE ON THE VOLATILE OIL OF HOPS.

FRANK RABAK, CHEMICAL BIOLOGIST, OFFICE OF DRUG-PLANT INVESTIGATIONS, BUREAU OF PLANT INDUSTRY, U. S. DEPT. OF AGRICULTURE.

Among the many factors which tend to influence the composition of volatile oils, geographical source, with its attending conditions of climate and soil, is of noteworthy importance. It is a generally accepted fact that a close relationship exists between the growth of a plant with the formation of its constituents, and climatic factors such as, heat, light, moisture, dryness and soil conditions. With regard to volatile oils in general, a number of factors may produce variation in aroma or quality. This geographical location may influence the aromatic property of an oil as attested by Jeancard and Satie,[1] who state that the locality in which lavender, thyme, rosemary and roses are grown has considerable effect upon certain constants of the oils. According to Bonnier,[2] altitude, light, hygrometric conditions and temperature also affect the plant functions and thus affect its composition. Condition of the soil is also important according to Lamothe,[3] who states that soil fertilized with superphosphates increases the esters of lavender oil. In experiments with peppermint Charabot and Hebert[4] have shown that soil treated with fertilizers produce plants richer in esters and odor-bearing compounds.

Since the conditions mentioned affect the composition of a number of volatile oils, it may be easily comprehended that similar effects may be produced on hops grown in separate localities under different conditions. Furthermore, since the effects on other oils have been noted chiefly in the esters or odor-bearing constituents, it is very probable that the volatile oil of hops would suffer like changes in ester content. For the purpose of ascertaining the truth of the above assumption the following investigation was undertaken.

In order to determine whether any differences exist in the volatile oils of hops, the physical and chemical constants were carefully determined. The physical properties, specific gravity, optical rotation, refraction, and solubility in alcohol are most important in revealing differences due to variation in composition.

[1] Jeancard, P., and Satie, C. La Chimie des Parfums en 1908. Revue Générale de Chimie pure et appliquee Tome 12, p. 181, 1909.

[2] Bonnier, G., Recherches experimentales sur l'adaption des plantes au climat Alpin. Annales des Sciences Naturelles Botanique. Serie 7, Tome 20, p. 217, 1894.

[3] Lamothe, L., Lavender and its Oil. American Perfumer and Essential Oil Review. Vol. 3, p. 128, 1908.

[4] Charabot, A., and Hebert, A. Bulletin du Jardin Colonial. Vol. 27, 1902, 3rd series, pp. 224-914.

Among the chemical constants the ester value is possibly of the most importance because of its close relationship to the aroma of the oil.

For the purpose of learning whether any constant differences exist in the various hops, it was planned to compare the oils distilled from hops grown in the hop-producing sections of the United States with the oil distilled from an authentic sample of imported hops, all of the samples to be from hops grown during the same season. The sections chosen in the United States were California, Oregon, Washington and New York. The imported hops were from Bohemia.

A comparison of the oils obtained from the hops during a single season would give results which would be valuable in determining differences for that particular season, but it was also important to ascertain whether the same differences occurred from year to year. Therefore the experiments were carried on for several successive seasons and the oils obtained from the hops of any one locality were compared with those from the same locality during these successive years. This procedure permitted an absolutely fair comparison by which similarities or differences in the properties of the oils could be easily followed and fluctuations readily noted.

The usual method of steam distillation was applied for the extraction of the volatile oils from the various samples of hops. The conditions of distillation were practically identical in all cases, each sample being distilled until no more oil was noticeable. The California hops were from Perkins, Cosumne, Ukiah, and Wheatland. The Oregon samples were from Independence, the Washington samples from Chehalis, and the New York samples from near Waterville. All were representative samples of commercial sulphured hops. The imported hops were from Saaz, Bohemia.

### THE YIELDS OF OIL FROM VARIOUS HOPS.

The yields of oil from various hops during the four successive seasons are given in the following table:

*Yields of Volatile Oil from Various Hops During the Years 1906 to 1909, Inclusive.*

| Source of Hops. | 1906 | 1907 | 1908 | 1909 | Average. |
|---|---|---|---|---|---|
| | Percent. | Percent. | Percent. | Percent. | Percent. |
| California: | | | | | |
| Perkins | ..... | 0.2 | 0.38 | 0.43 | 0.336 |
| Cosumne | ..... | 0.32 | 0.24 | 0.42 | 0.326 |
| Ukiah | ..... | 0.23 | 0.53 | 0.28 | 0.346 |
| Wheatland | ..... | 0.21 | 0.20 | 0.44 | 0.283 |
| Oregon | 0.34 | 0.20 | 0.32 | 0.30 | 0.290 |
| New York | 0.32 | 0.16 | 0.14 | 0.15 | 0.192 |
| Washington | ..... | ..... | 0.36 | 0.38 | 0.370 |
| Imported (Saaz) | 0.45 | 0.32 | 0.23 | 0.24 | 0.310 |

Considerable variation exists in the yields of oil from the different California hops, not only among the different samples of any one season, but also among the same hops during successive seasons. The average yield of oil from the California hops during the seasons recorded in the table was 0.32 percent.

The Oregon hops which were distilled during the four successive years showed an average oil content of 0.29 percent, which is a trifle less than the average California sample.

The New York hops with an average during the four years of 0.192 percent of oil were noticeably lower in oil content than any of the other hops distilled.

The Washington hops which were distilled only during two seasons appear to possess the highest percentage of oil, the average being 0.37 percent.

The imported hops distilled from the crops of 1906, 1907, 1908, and 1909, showed an average yield of 0.31 percent of oil, considerable change appearing from season to season.

This variability of the oil content may be ascribed to varying conditions of climate and soil as well as to ripeness and drying of the hops, which would affect the formation of the oil in the plant. Slight differences in yield of oil would not necessarily influence the quality since the same proportion of odoriferous constituents may still be present.

PHYSICAL PROPERTIES OF THE VARIOUS HOP OILS.

The physical properties of the oils permit a somewhat better means of comparison. The properties of color, odor and taste, which are apt to disclose only slight differences, are not discussed. The specific gravity, refractive power and solubility, each of which can be accurately measured, are of much greater importance, although even these properties are usually entirely inadequate for detecting any constant differences in the oils. In all cases the oils were too dark to permit making determination of the optical rotation which is often useful in detecting certain differences in composition. The following tabulations show the differences in the physical properties of the various hop oils distilled during the seasons 1907, 1908, and 1909:

*Physical Properties of Various Hop Oils Distilled During Several Successive Seasons.*

Specific Gravity at 20° C.

| Source of Hops. | 1907 Crop. | 1908 Crop. | 1909 Crop. |
|---|---|---|---|
| California: | | | |
| Perkins | 0.821 | 0.838 | 0.8316 |
| Cosumne | 0.821 | 0.8395** | 0.842 |
| Ukiah | 0.821 | 0.831** | 0.839** |
| Wheatland | 0.828 | 0.8443 | 0.8358 |
| Oregon | 0.8343 | 0.838 | 0.8433 |
| New York | 0.859* | 0.834* | 0.8747* |
| Washington | ..... | 0.850 | 0.8464 |
| Imported (Saaz) | 0.852* | 0.821* | 0.858* |

* Specific Gravity at 24° C.
** Specific Gravity at 23° C.

Index of Refraction at 20° C.

| Source of Hops. | 1907 Crop. | 1908 Crop. | 1909 Crop. |
|---|---|---|---|
| California: | | | |
| Perkins | 1.4838 | 1.4783 | 1.4716 |
| Cosumne | 1.4825 | 1.4724 | 1.4733 |
| Ukiah | 1.4890 | 1.4737 | 1.4718 |
| Wheatland | 1.4870 | 1.4753 | 1.4743 |
| Oregon | 1.4802 | 1.4730 | 1.4705 |
| New York | 1.4804 | 1.4756 | 1.4800 |
| Washington | ..... | 1.4763 | 1.4734 |
| Imported (Saaz) | 1.4905 | 1.4852 | 1.4829 |

*Solubility.**

(Amount of Oil Dissolved in 3 Volumes of 94 percent alcohol.)

| Source of Hops. | 1907 Crop. | 1908 Crop. | 1909 Crop. |
|---|---|---|---|
| California: | | | |
| Perkins | 0.55 volume oil, turbid yellowish residue. | 0.7 volume oil, turbid. | 0.8 volume of oil. |
| Cosumne | 0.5 volume of oil with whitish residue. | 0.85 volume of oil, brownish residue. | 0.8 volume oil. |
| Ukiah | 0.35 volume oil, slight turbidity. | 0.85 volume oil, turbid | 0.95 volume oil. slightly turbid with reddish residue. |
| Wheatland | 0.35 volume oil, yellowish residue. | 0.75 volume oil, brown residue. | 0.7 volume oil. |
| Oregon | 0.65 volume oil, turbid, yellow residue. | 0.9 volume oil. | 1 volume oil. |
| New York | 0.85 volume oil, brown residue. | 0.85 volume oil. | 0.8 volume oil, light brown residue. |
| Washington | ..... | 0.85 volume oil, turbid. | 0.9 volume oil. |
| Imported (Saaz) | 0.75 volume oil, slightly turbid. | 0.5 volume oil, yellowish viscous residue. | 0.75 volume oil. slightly turbid. Dark brown viscous residue. |

*Solubility of 1907 crop determined after two years; 1908 crop determined after one year.

The densities of the California oils bore a close relationship during individual seasons, differing somewhat from season to season. This would seem to indicate that the approximate composition during any one season was about the same in the several oils. The oils with the highest general specific gravity were those from New York hops, which averaged 0.8554 at 24° C. The Washington, imported, Oregon, and California oils followed in order. It is generally acknowledged that the specific gravity is modified by the composition of the oil but it is doubtful whether the differences noted above would cause any remarkable change in the quality of the oil. A high specific gravity would usually be accompanied by a larger percentage of high-boiling constituents and vice versa.

From the table it will be observed that the oils from imported hops possess higher refractive indices than any of the other oils. This again may be due to the presence of a somewhat higher percentage of highly refractive constituents in these oils. The refraction of the oils from the 1907 crop was higher in most cases than that of the two following years, probably because the constants of the oils from this crop were not determined until 1909, showing that a change had taken place in the oils while aging.

The solubility of hop oil is influenced considerably by the percentage of terpenes and sesqui-terpenes present, the presence of which tend to decrease the solubility in alcohol, while high content of oxygenated compounds increases it. Owing to the preponderance of the former in hop oils and the difficulty thereby encountered in obtaining comparative results, a deviation was made from the usual method for determining solubility. One volume of oil was thoroughly shaken with three volumes of 94 percent alcohol in a graduated cylinder after which the resinous insoluble matter was centrifuged. The amount of insoluble matter could then be easily read on the bottom of the cylinder and the amount of dissolved material readily calculated.

Apparently the most soluble oil among the number was the oil from Oregon

hops of the 1909 crop, one volume of this oil dissolving completely in three volumes of 94 percent alcohol, the oil from the 1908 crop being almost as soluble. The Washington and New York oils from the crops of 1908 and 1909 were slightly less soluble than the Oregon oils. The California oils of these two seasons were a trifle less soluble than those from Washington and New York hops, while the imported oils appeared to be the least soluble.

The much lower solubility of the 1907 oils was due to the fact that the determinations were not made until two years after distillation. Although the oils had been kept in well-filled bottles and well-protected from light, decomposition had ensued which resulted in the formation of less soluble constituents thus decreasing the solubility of the oils. This plainly shows the effect of age on the solubility of the oils.

From the results obtained, it would appear that the oils with the highest solubility probably contained a larger percentage of oxygenated compounds and a lower percentage of terpenic compounds than the less soluble oils.

### CHEMICAL PROPERTIES OF THE VARIOUS HOP OILS.

In order to make a better comparison of the several oils with regard to their aromatic quality, determinations were made of the acid, ester and saponification numbers.

A number of factors may tend to influence the acid value. Freshly distilled oils are in most instances low in free acidity, while old oils or oils distilled from old material usually possess a larger quantity of free acids. Improper conditions of drying and storing have a tendency to cause changes to take place which result in the formation of free acids and thereby increase the acid numbers.

As previously stated, the ester values of oils are subject to marked changes due to conditions of climate, soil, etc. This value in hop oils may also be affected by conditions under which the material is dried and stored. The stage of growth and development of the plant as influenced by geographical location may also be a strong factor in modifying the ester content.

The saponification number being the sum of the acid and ester numbers should indicate much the same differences, as shown by the ester numbers. A determination of free alcohols in hop oils was not feasible because of the inability to acetylize the oil quantitatively.

The acid, ester and saponification numbers of the oils from the American and foreign hops are recorded as follows:

*The Acid, Ester and Saponification Numbers of Hop Oils Distilled During Several Seasons.*

Acid Numbers.

| Source of Hops. | 1906 | 1907 | 1908 | 1909 | 1910 | Average |
|---|---|---|---|---|---|---|
| California: | | | | | | |
| Perkins | ..... | 0 | 1.5 | 1.1 | ..... | 0.86 |
| Cosumne | ..... | 0 | 2.4 | 2.9 | ..... | 1.76 |
| Ukiah | ..... | 0 | 1.1 | 1.8 | ..... | 0.96 |
| Wheatland | ..... | 2.3 | 2.0 | 1.4 | ..... | 1.9 |
| Oregon | 5.5 | 1.6 | 1.0 | 2.8 | ..... | 2.7 |
| New York | 4.8 | 3.6 | 2.1 | 2.5 | ..... | 3.25 |
| Washington | ..... | ..... | 1.0 | 1.5 | ..... | 1.25 |
| Imported (Saaz) | 1.5 | 1.5 | 1.0 | 3.0 | 3.1 | 2.02 |

Ester Numbers.

| Source of Hops. | 1906 | 1907 | 1908 | 1909 | 1910 | Average |
|---|---|---|---|---|---|---|
| California: | | | | | | |
| Perkins | ..... | 42 | 47 | 47.1 | ..... | 45.5 |
| Cosumne | ..... | 45 | 46 | 51 | ..... | 47.3 |
| Ukiah | ..... | 40.8 | 44 | 51 | ..... | 45.2 |
| Wheatland | ..... | 50 | 45.5 | 41 | ..... | 45.5 |
| Oregon | 72 | 57 | 50.2 | 56 | ..... | 58.8 |
| New York | 44 | 61 | 47 | 51.8 | ..... | 50.9 |
| Washington | ..... | ..... | 51.8 | 53.8 | ..... | 52.8 |
| Imported (Saaz) | 12.6 | 20 | 36 | 28.6 | 20.4 | 23.5 |

Saponification Numbers.

| Source of Hops. | 1906 | 1907 | 1908 | .909 | 1910 | Average |
|---|---|---|---|---|---|---|
| California: | | | | | | |
| Perkins | ..... | 42 | 48.5 | 48.2 | ..... | 46.2 |
| Cosumne | ..... | 45 | 48.4 | 53.9 | ..... | 49.1 |
| Ukiah | ..... | 40.8 | 45.1 | 52.8 | ..... | 46.2 |
| Wheatland | ..... | 52.3 | 47.5 | 42.4 | ..... | 47.4 |
| Oregon | 77.5 | 58.6 | 51.2 | 58.8 | ..... | 61.5 |
| New York | 48.8 | 64.6 | 49.1 | 54.3 | ..... | 54.2 |
| Washington | ..... | ..... | 52.8 | 55.3 | ..... | 54.0 |
| Imported (Saaz) | 14.1 | 21.5 | 37 | 31.6 | 23.5 | 21.5 |

The oils in order of their average acidity were as follows: New York, Oregon, imported, California, and Washington. In every instance the New York oils showed comparatively high acidity. The average acidity of the New York and Oregon oils was probably somewhat high as it was considerably augmented by the high acid number of the oil from 1906 crop which was distilled from hops which were not fresh as were those from 1907, 1908, and 1909 crops. The oils with lowest acidity were from California and Washington hops, while the imported hops occupied an intermediate position.

The ester numbers revealed most striking similarities and dissimilarities, not only during one season, but for several successive seasons. It was to be expected that the oils from the hops during any one season would show differences but that these same differences should appear during three and four and even five successive seasons was most surprising.

The oils from the imported hops were conspicuous because of the fact that the data for the several seasons showed the ester content to be only about one-half as great as the ester content of the oils from the California, Oregon, Washington and New York hops. Besides the samples recorded, a cold storage sample of Saaz hops of the 1906 crop distilled one year later gave an oil with an ester number of 24. Three samples of imported hops of the 1910 crop, namely, Dauber, Auscher and Oesterreich Gewächs hops, possessed the ester numbers 15.7, 21.3, and 18, respectively. In all nine samples of imported hops from five seasons gave oils with uniformly lower ester content than American hops.

The close relationship of the ester numbers of the California oils during the seasons of 1907, 1908 and 1909, is very evident. The general average ester

number of the California oils was 45.5, as compared with 50.9 for New York, 52.8 for Washington, 58.8 for Oregon, and 23.5 for the imported.

In case of the foreign oils the ester numbers, which are a measure of the odorous constituents, would seem to point to consistently lower content of these compounds.

The saponification numbers which represent the total acids and esters in the oils presented practically the same constant differences and similarities brought out by comparison of the ester numbers.

While it is not known whether the ester numbers would continue lower indefinitely in case of the foreign oils, it may be assumed that such would be the case, since the authentic samples distilled during five seasons showed abnormally low values as compared with the American oils. In a like manner also it may be assumed that the high ester numbers of the American oils would continue indefinitely since they were quite remarkably constant during the seasons in which the experiments were carried on.

### THE RELATION OF THE VOLATILE OIL TO THE SOURCE OF THE HOPS.

A comparison of the fractions resulting from the fractionation of each of the above oils both with regard to physical and chemical constants brought out the same relationships as were shown to exist in the oils themselves. It is, of course, impossible to discuss these results in detail in the short space of this paper. However, from the data presented it is clearly evident that the geographical source of hops has a pronounced effect upon the volatile oil and particularly upon the ester content. The differences noted in the oils appear to be fairly constant from season to season, not only in the physical properties but also in the more important chemical properties. Not only do hops of foreign origin produce oils noticeably dissimilar in some of their properties from the American oils, but hops grown even in separated sections of the United States yield oils with more or less constant differences from year to year. In general, it may be stated with some degree of certainty that the geographical source of hops exerts a decided influence upon the composition of the oils, especially as regards the ester content. Furthermore, it seems highly probable that the geographical source of hops may be indicated by the ester numbers of the oil distilled from the hops since the experiments have shown that the ester numbers of the oils from hops of any particular source or season are very similar.

# THE PHYSIOLOGICAL ACTIVITY OF "ERGOTIN" AND POWDERED EXTRACT OF ERGOT.

CHAS. C. HASKELL, B. A., M. D.

There now seems little question as to the therapeutic value of the official fluid extract of ergot. It is sometimes desirable, however, to have solid or semi-solid ergot preparations in a more concentrated form than the crude drug, and it is also often advantageous to secure the active principles in a water-soluble form. These considerations, however, should have no weight, if it is learned that the process of manufacture of such special preparations destroys or greatly lessens the therapeutic activity originally possessed by the crude drug.

Two such "special preparations" have recently been the subject of investigation in this laboratory, and it seems of interest to report the results secured.

The first of these preparations is so-called "Ergotin." It is made by treating powdered ergot with benzin to remove the oils; air drying in order to free from benzin; and percolation with water. The percolate is reduced to a syrupy consistence at 90° to 120° C. and alcohol added. The resulting precipitate is removed by filtration and the filtrate reduced to a semi-solid extract at 90° to 120° C.

The second preparation is a powdered extract made by percolation of ground benzin-extracted ergot with 50 percent alcohol; reduction of percolate to a solid in vacuum dryer and addition of approximately an equal quantity of benzin-treated powdered ergot.

From theoretical considerations, it would seem that little, if any, ergotoxin would be contained in the "ergotin" and what activity it possesses would be due to the amines described by Barger, Dale, Kraft, and others. The powdered extract, however, consists of about one-half powdered drug and the remainder of an alcoholic extract, so one would expect all the active constituents to be present, unless the benzin or the elevated temperature exercised a deleterious influence.

Ergot still finds its chief field of usefulness as an oxytoxic; consequently, any laboratory attempt to estimate the therapeutic efficiency of the drug should be based upon a determination of its oxytoxic power. It has been shown conclusively that a measurement of the pressor-activity of ergot gives no reliable information of the value of the drug as a stimulant to uterine contractions, and it is illogical and useless to make such tests if the drug is to be used in obstetrical practice. It is not improbable, however, that blood-pressure tests upon dogs may give reliable data as to the efficacy of the drug as a circulatory stimulant for man.

The excellent work of Edmunds and Hale has demonstrated that the cock's comb test gives results closely paralleling those secured when the drug is tested upon the uterus of an experimental animal. These authors point out that the cock's comb method is simple and allows of considerable accuracy.

During the past few months, we have had occasion to examine twenty-four samples of crude ergot; four samples of ergotin; and nine samples of powdered extract of ergot. In every instance, when a large enough dose was given intramuscularly to white leghorn cocks, bluing of the comb, diarrhoea and dyspnœa

Figure I. Showing the contractions of a rabbit's uterus after the intravenous injection of Solid Extract of Ergot.

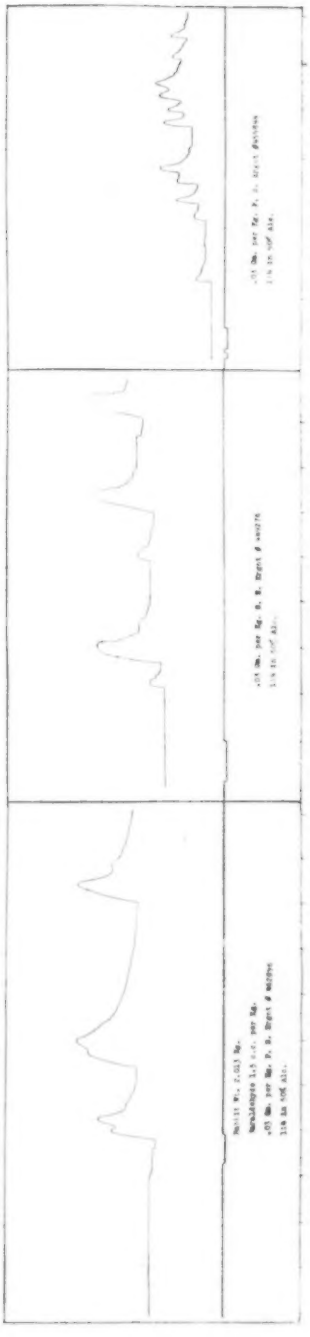

Figure II. Showing the contractions of a rabbit's uterus after the intravenous injection of Po. E. Ergot and of Sol. E. Ergot.

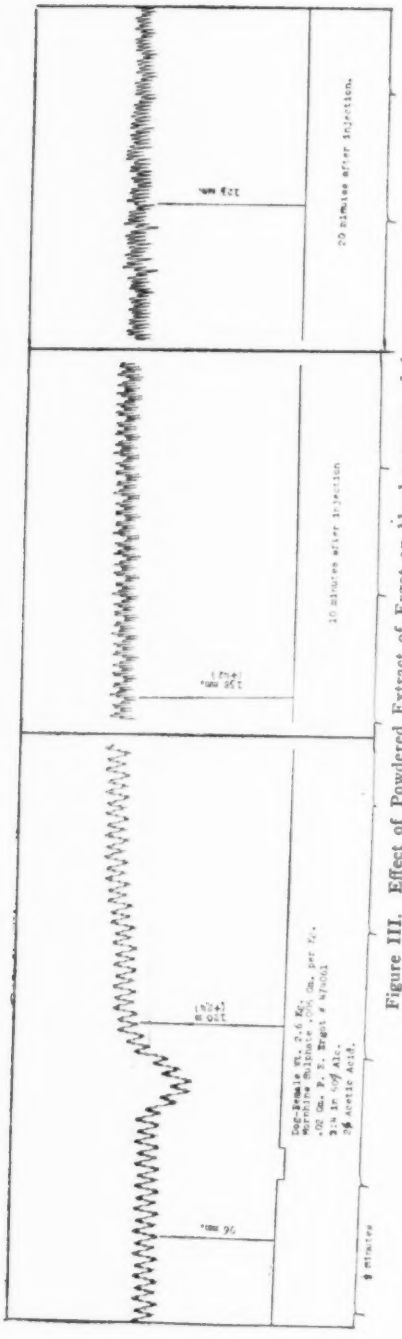
20 minutes after injection.
10 minutes after injection
Dog-female Wt. 7.6 Kg.
Morphine Sulphate .005 Gm. per Kg.
.02 Gm. P. E. Ergot # 478061
3.5 cc 50% Alc.
5% Acetic Acid.
5 minutes

Figure III. Effect of Powdered Extract of Ergot on blood pressure of dog.

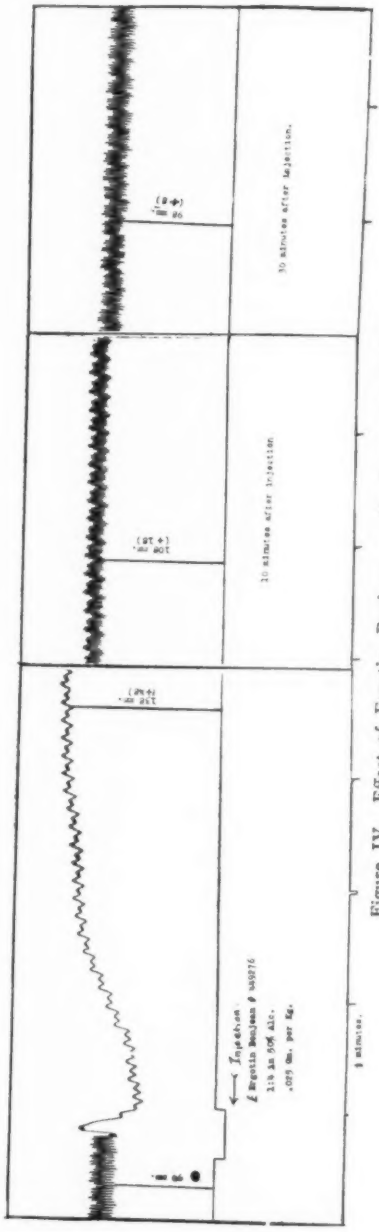


Figure IV. Effect of Ergotin, Bonjean, on blood pressure of dog.

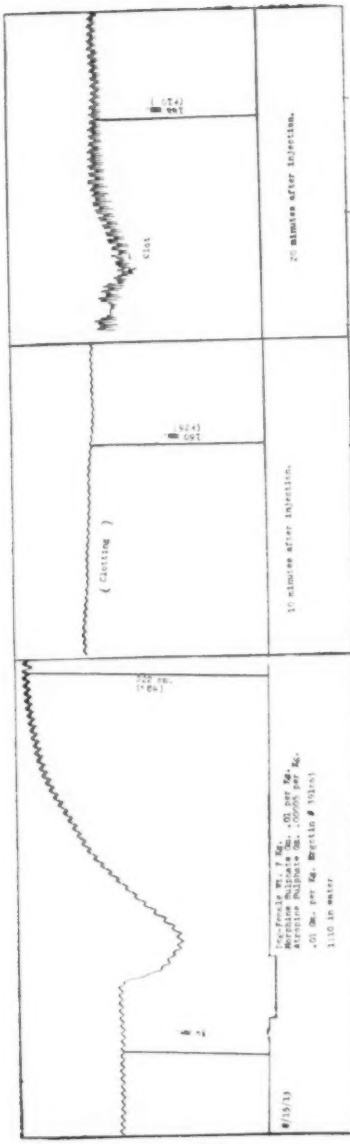


Figure V. Effect of Ergotin, Bonjean, in small amount on blood pressure of dog.

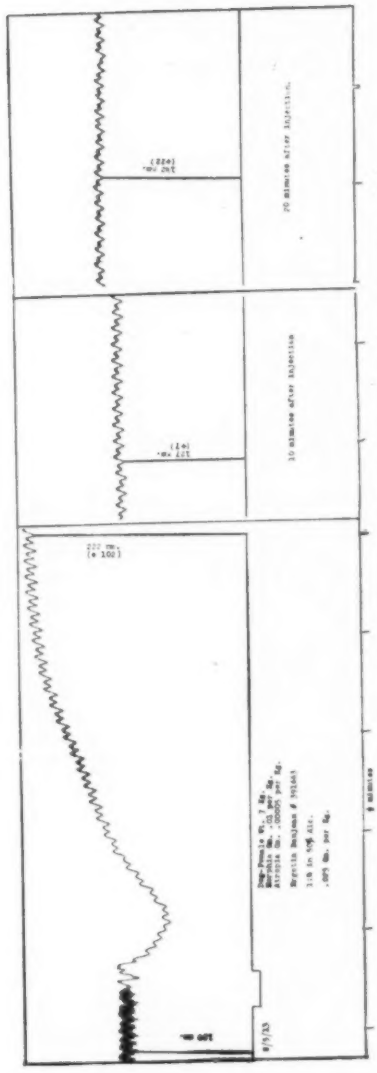


Figure VI. Effect of Ergotin, Bonjean, in medium amount on blood pressure of dog.

resulted; the symptoms produced by each preparation being practically identical. It seemed desirable, however, to test some of the samples of "ergotin" and powdered extracts upon the uterus of a lower animal. Consequently, rabbits were used in the way described by Cushny, and a marked effect was produced by these preparations in every instance in which they were employed. The tracings, represented in Figures 1 and 2, illustrate the results secured.

These figures do not show the entire records, as the uterus was allowed to return to and remain in, a practically quiescent state for at least one-half hour before the drug was injected.

While feeling that blood-pressure experiments gave no positive information as to the value of the preparations as stimulants of the uterus, nevertheless a number of tests were made upon dogs, using the method of Wood and Hofer, except that 10 mgms. of morphine per kilogram were administered and the dogs also received a small dose of atropine, as suggested by Edmunds and Hale. The following tracings, Figures III and IV, show that these preparations have a marked pressor action.

From the evidence presented, it seems fair to assume that "ergotin" and powdered extract of ergot have the characteristic "ergot" action. It is of interest, however, to learn whether the full amount of drug activity is retained in these preparations.

In the manufacture of "ergotin," approximately six pounds of drug are used to finish one pound of extract. For the powdered extract eight pounds of drug usually furnishes one pound of extract. Consequently, "ergotin" should be six times as active and the powdered extract eight times as active as the crude drug.

Of the twenty-four samples of crude ergot examined by the cock's comb test, all were capable of causing bluing of the comb when given in a dose of 1 gram per kilogram. Of the nine samples of powdered extract examined, a dose of 0.25 gram per kilogram was efficient in all instances. Of the four samples of "ergotin" 0.25 gram per kilogram was efficient in two cases; while 0.3 gram was required in the other two. From this, it seems that the powdered extract is about four times as active as the crude drug; while "ergotin" is, roughly, about three and one-half times as active.

By blood-pressure experiments, however, a different relation is apparent. We have found that 0.1 cc. per kilogram is the optimum dose of fluid extract; that is, this dose usually causes the maximal rise of pressure. With "ergotin," however, the optimum dose seems 0.0125 gram per kilogram; or about one-eighth that of the fluidextract. Cronyn and Henderson have pointed out that large doses of ergot produce poor pressor response, and this is well illustrated by the following tracings, Figures V, VI and VII, where it is seen that with the same preparation of Ergotin (No. 391663) a small injection of 0.01 gm. per kilogram sustains an increased blood pressure much better than does an injection of 0.025 or of 0.05 gm. per kilogram. In fact the blood pressure twenty minutes after the injection of 0.05 gm. per kilogram is actually below its initial pressure. This may serve to explain the poor results that have been secured by others in testing the pressor action of these preparations.

In conclusion it may be said that:

1. "Ergotin" and powdered extract of ergot are capable of causing bluing of

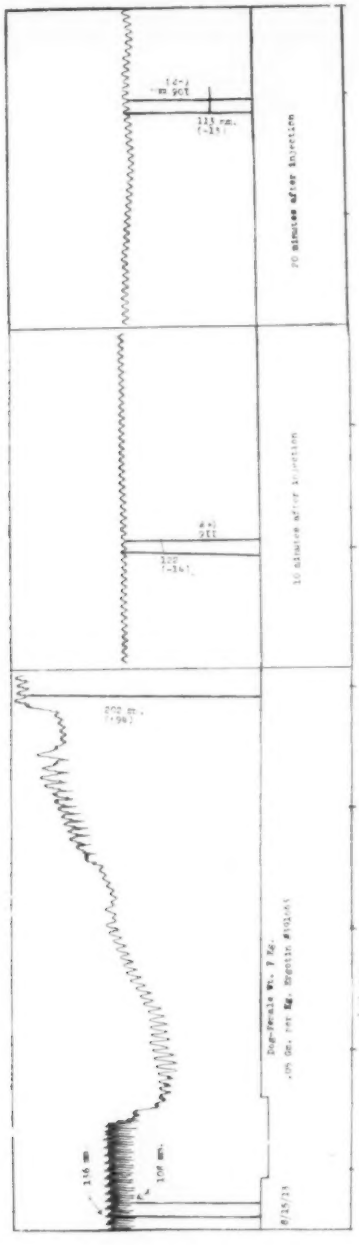

Figure VII. Effect of Ergotin, Bonjean, in large amount on blood pressure of dog.

the cock's comb; contraction of the rabbit's uterus; and rise of the dog's blood-pressure.

2. There is apparently a considerable loss in the manufacture of these preparations, of those substances influencing the uterine movements, while there is but slight loss in the pressor-activity originally possessed by the crude ergot.

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# STERILIZATION.

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A knowledge of sterilization is becoming more and more important to the pharmaceutical profession as the administration of medicines by the sub-cutaneous and intravenous routes increases in popularity.

The purpose of sterilization in pharmacy is to destroy such forms of microbic life as may exist in medicinal preparations and the various containers, etc., used in handling and dispensing them. Of the innumerable living things that may be found in crude drugs, only the microscopic forms, such as yeasts, molds and bacteria usually escape elimination in the course of manufacture. It is necessary to destroy molds and yeasts, because their growth may result in fermentation or other forms of decomposition, with deterioration, and the production of harmful by-products; but far greater in importance, are the bacteria, which have an additional property only rarely exhibited by yeasts and molds—that of multiplying in the animal body and causing disease.

These microscopic organisms are ubiquitous in nature; one can think of few places where they may not be found. Some of them will grow only upon living tissues (parasites), others will grow only upon dead matter (saprophytes). There are a few species which seem able to multiply even in distilled water, depending upon gases absorbed from the air for their nourishment. Some of the bacteria die quickly when removed from media favorable to their growth, others are so tenacious of life that they may exist for years and possibly for centuries in unfavorable surroundings.

In considering the problems of sterilization it is these latter bacteria to which we are compelled to give especial attention. When organisms of this class find themselves in a medium unsuited to their rapid growth, they go into a state that may be considered a kind of hibernation. The vital part of the bacterial cell is collected within a very resistant capsule, which, with its contents, is known as a spore. The spore state is not a means of reproduction in the sense of multiplication, it is merely a means of self-preservation. One bacillus makes one spore, and one spore makes one bacillus. Therefore, while spores are like seeds in preserving the essential vitality of the cell, they differ in that seed formation is chiefly a reproductive (multiplying) function.

Some spores are able to withstand heat to the boiling point of water for several hours, while bacteria not in the spore state are killed when heated to 60° C. for less than one hour. This difference in the degrees of heat required for killing spores and bacteria, also holds with regard to other germicidal influences. Spores are far more resistant, to phenol for instance, than are non-sporogenic bacteria. The state of the preparation to be sterilized with regard to moisture, is of great importance, since bacteria which are entirely dry may be heated to very far beyond the boiling point of water without killing them, an important point in discussing methods for sterilizing tablets and powders.

Fortunately there are few common sporogenic bacteria which cause disease if they gain entrance to the uninjured intestinal tract.

Whether a remedy is to be administered upon the unbroken skin or mucous membranes, or enterally, that is by mouth or by rectum, or parenterally, under the skin or into a vein—these differences are of fundamental importance. For local application or enteral administration, approximate sterility is usually sufficient, but for parenteral injection or for use in a surgical operation, complete asepsis is requisite. For instance, the tetanus bacillus taken by mouth, is not likely to do any harm, but injected beneath the skin, will, under favorable circumstances, cause tetanus or lock-jaw. By the term parenteral injection is meant, as I have just indicated, the internal administration of a remedy by other than the gastro-intestinal route, that is sub-cutaneously, intravenously, intraperitoneally, intramuscularly, intraspinally, etc.

Unless remedies intended for local or enteral administration are suspected to contain disease-producing bacteria, sterilization is not generally thought of in connection with them, except in so far as it concerns their preservation. For this purpose the addition of chemical substances is simpler, and since their action is continuous they are more efficient than heat or filtration. This is well exemplified by the fact that, with few exceptions, pharmaceutical preparations, e. g., tinctures, fluid extracts, syrups, etc., contain sufficient alcohol, sugar or other preservative to prevent decomposition through bacterial growth. It is thus apparent that the chief concern we have with sterilization is the preparation of remedies intended for parenternal use.

By sterilization we mean the destruction or removal of every form of reproductive life. To accomplish this we have several methods, physical, chemical and mechanical. The physical methods are heat, electricity and light,—sunlight, ultra-violet rays, etc.

Chemical sterilization is accomplished by the use of such substances as phenol, corrosive sublimate, etc.

The mechanical methods for sterilization of greatest service are filtration, and centrifugation.

*Heat.* The *naked flame* may be used for sterilizing certain instruments, platinum vessels, spatulas, and small pieces of glassware. A Bunsen burner is generally used for this purpose.

*Dry heat* may be used for the sterilization of glass bottles, and other glass vessels of various kinds, for powders that are not injured by a high degree of heat, and, where an autoclave is not available, for the sterilization of cotton. It cannot be used for organic or volatile substances or for aqueous solutions. To prepare them for sterilization, bottles and flasks are stoppered with cotton and, as an extra precaution, they may have a piece of paper tied over their mouths before being placed in the oven. They must be perfectly dry. Other pieces of glassware may be wrapped in filter paper or in ordinary Manila paper.

The best arrangement for sterilizing by dry heat is the dry-wall sterilizer of the Lautenschlager pattern. This is a special laboratory apparatus heated by gas, with the walls so arranged that the hot air is kept in motion and approximately, the same heat is maintained in all parts of the oven. A small dry-wall sterilizer is not expensive, but, since the desired heat may be obtained in an ordinary bake-oven, it is likely that in pharmacies, where a great deal of work requiring sterilization is not done, the pharmacist will use the kitchen range, and

he may do so with perfect safety. For small pieces of glassware it is the rule to consider sterilization accomplished when the paper wrapping has started to char. A precaution that must be noted, however is, that, if the oven is extremely hot, the paper may char almost immediately, before the heat has had time to penetrate to the vessel. In using the dry-wall sterilizer, it is customary to run the heat up to 180° C., and continue it at this point for two hours.

*Steam and boiling:* The method which has by far the widest field of application is sterilization by steam. There are two methods: (1) by steam under pressure in a closed chamber called an autoclave, (2) by a double walled hood, in which materials are subjected to streaming steam without pressure.

Steam has much greater penetrating power than dry air. Bacteria entirely dry are sometimes not killed even by heating them to a temperature of 150° C., while all bacteria are destroyed in steam under pressure at 120° C. The best apparatus for sterilizing in streaming steam is the Arnold sterilizer. This consists of a pan with a thin false bottom into which water flows and comes in contact with the heat in such a thin layer that it is almost immediately converted into steam. As the steam passes up through the central opening, water trickles down through small holes at the corners of the pan. The sterilizing chamber has a double wall, which helps to conserve the heat. The inside chamber is maintained at a temperature of about 100° C. for at least twenty minutes after the materials being sterilized have reached this temperature. Such a temperature is not sufficient to kill spores and in order to destroy them the "Tyndall," or discontinuous method, must be used. That is to say, substances to be sterilized by streaming steam are heated for twenty minutes on three successive days. The idea is that all active bacteria are killed on the first day; during the period after heating, until the next day, if there is any nourishment present, the spores develop into bacteria and are killed at the second heating. Any spores that may have escaped the second heating are pretty certain to have developed by and will be killed on the third day. While this is the explanation given by some writers, others think that the spores are gradually weakened by the repeated heating, until they are finally destroyed completely on the third day. Fluids that will not stand the temperature of the autoclave, but which will stand boiling may be efficiently sterilized in the Arnold sterilizer by the discontinuous method, provided they contain sufficient nutrient material to favor the development of any possible spores, otherwise the method may fail and filtration, with or without the use of an antiseptic, must be employed. The pharmacist who does not have this special apparatus, can secure the same result if the bottles or flasks containing the fluid to be sterilized are placed in water in a covered vessel, such as a wash boiler or a covered saucepan. The vessels containing the fluid to be sterilized should be raised from the bottom of the pot by a piece of woven wire or something of the kind, and their tops should be well protected so that the cotton stoppers will not get wet.

A still simpler method is to place the fluid in an Erlenmeyer or Florentine flask, which has been sterilized by dry heat, and boil it for fifteen to twenty minutes over the naked flame on three successive days. This method is open to the objection that there is considerable evaporation and therefore it cannot be used if the original bulk of the fluid must be maintained. If there is no objection to it,

a surface coating of liquid paraffin will prevent evaporation, unless the boiling is too vigorous.

It is well known that the boiling point of mineral oils is much greater than the boiling point of water. These may be sterilized by heating them over the naked flame, to 160° C., in a suitable flask.

*Steam, under pressure* in a closed chamber, known as an autoclave, is the most useful means for sterilizing the ordinary culture media employed in bacteriological laboratories. This is the best method for sterilizing dressings, physiological saline solution, and other fluids not injured by the autoclave temperature. For sterilization in the autoclave, the temperature is maintained at 115° C. to 120° C. under a pressure of from ten to fifteen pounds for twenty to forty minutes.

Fluids not intended for parenteral administration, such as foods of various kinds, that may be contaminated by disease-producing bacteria, are efficiently sterilized by Pasteurization. This is accomplished by heating to a temperature of at least 60° C. maintained for one-half to one hour, the time depending upon the degree of heat used. A temperature so low as 56° C. is sufficient to kill many non-sporogenic bacteria and substances destroyed by a degree of heat greater than this, may usually be sterilized by subjecting them to this temperature, for about one-half hour, from five to seven successive days. In some laboratories the blood serum mixture used for the diagnosis of diphtheria is sterilized by this method.

*Sterilization of Fluids in Sealed Capsules:* It is possible for the pharmacist to dispense solutions efficiently sterilized, without the use of any apparatus other than a vessel that may be used as a water bath. The solutions that are to be dispensed, however, must be placed in glass containers hermetically sealed—the most useful form being the bottle with a long narrow neck commonly called an ampoule. These, stoppered with cotton and wrapped in paper, or placed in a metal box, are sterilized by dry heat, maintained at 180° C. for two hours. After the fluid to be dispensed is filled into them, through a narrow tube or by vacuum, the necks of the ampoules are sealed in a blow-pipe flame. They may then be sterilized at any temperature their contents will withstand. For instance if it is a question of a cocain solution, the ampoules may be heated to about 60° C. for one hour on seven successive days, at the end of which time they should be sterile—cocain hydrochlorid is said to withstand a temperature of 70° C. without decomposing. If the substance in solution will withstand 100° C., the ampoules may be boiled for one-half to one hour on three successive days. Should a higher temperature be unobjectionable, the autoclave conditions may be obtained by the use of a strong solution of calcium chlorid or other salt in the water bath or one may use a mineral oil. If liquid paraffin is used the ampoules are easily cleansed after sterilization by rinsing them in ether.

*Chemical Methods:* The chemical methods for sterilization include the use of the well-known germicides, such as bichloride and oxycyanide of mercury, carbolic acid, liquor cresolis comp., formaldehyde, etc. There are times when solutions of these may be used in such strength that they will efficiently sterilize the substances in question. In by far the greater majority of instances, however, they can be added only in antiseptic strength, thus being used merely as preservatives. Cresol, the substance employed at present in practically all laboratories

as a preservative for biological materia medica, is used in various strengths ranging from 0.2 of 1 percent to 0.5 of 1 per cent combined with filtration for serums. In this strength it is only antiseptic. It does not become germicidal until we reach the minimum concentration in water of 2 percent, and even then considerable time must be allowed for its action upon spores. The sterilization of glass vessels, by allowing a strong disinfectant to remain in them cannot be recommended. Tiny scratches and fractures may still be large enough to protect bacteria, since capillary attraction might prevent the solution from coming in contact with them.

There are many well-known substances which are practically without germicidal value but which are efficient as antiseptics.These include boric and salicylic acids, camphor, thymol, etc. Glycerin in high concentration is quite efficient. Sugar is an efficient preserative and is widely used as such, especially in preserved foods.

*Filtration:* Properly used, and with an appreciation of its limitations, filtration is a method for sterilizing which may be of great value to the pharmacist, for the reason that by this means solutions may be freed from bacteria without the slightest change in their chemical composition. Filtration, of course, cannot be used for thick or syrupy liquids, nor can it be used for suspensions or emulsions of any kind. Many ingenious arrangements have been devised for the filtration of solutions required to be sterile. Some of these combine, in the apparatus, both filtering and filling devices.

*Contamination After Sterilization:* After a piece of apparatus or a preparation has been efficiently sterilized, proper precaution must be taken to prevent subsequent contamination. There are bacteria not only on *every object* with which it may come in contact, but also in the air. Consequently, if it be left uncovered, except under special conditions, contamination is almost certain to result. When fluids are transferred from one bottle or flask to another, the exposed part of the lip over which the fluid will run, must first be sterilized in the Bunsen flame. Such operations must be done only in specially constructed and protected rooms or under sterile or dust-proof hoods or other covers.

When a sterile fluid has been obtained in bulk, transferring it into smaller containers is one of the interesting problems confronting those responsible for the preparation of antitoxins and vaccines. Such operations must be carried on in specially prepared rooms or under dust-proof hoods. An ingenious and convenient substitute is the oven, as suggested by Professor Cook, or one may use a box lined with blotting paper saturated with a disinfectant solution. If one is expert, the transference may be made by pouring or by means of a sterile bulb pipette. These procedures are suitable for small quantities but for large amounts it is customary to use a graduated burette or a special contrivance, of which there are many on the market. In my experience a properly arranged burette is the most satisfactory filling apparatus for general purposes. In one of the larger manufacturing biological laboratories the filling of serums and vaccines is done in special rooms which are furnished with washed and filtered air. The rooms are disinfected with formaldehyde at least once a week and the operatives wear sterilized gowns and caps.

*Tests for Sterility:* In spite of the most approved *technique* and the most efficient apparatus, it may never be taken for granted that a fluid has been freed from living bacteria and has remained sterile throughout the process without proper bacteriologic controls. These controls must be such that they will meet every peculiar condition likely to influence the growth of bacteria in the solution. We read frequently of persons who make control cultures by placing a drop of the fluid upon nutrient agar—a solid culture medium. Sometimes fluids tested in this way, contain sufficient antiseptic to prevent the growth of bacteria which are present. This method is therefore faulty. Control tests must be made in a fluid medium, and the bulk of fluid must be sufficient to dilute the antiseptic contained in the substance under examination to such an extent that it can have no possible antiseptic power.

The contaminating bacterium may be an aerobe (i. e., one that requires oxygen for its growth) or it may be an anaerobe (one that requires the absence of oxygen). The control culture must afford conditions for the growth of bacteria of both kinds or two sets of controls must be made. Fortunately the latter is not necessary because the common fermentation tube affords conditions suitable for the growth of both varieties. The necessary condition is that the *bouillon* must have been freshly sterilized in order to drive off suspended or dissolved oxygen since this would prevent the growth of anerobic bacteria. After shaking the bottle containing the substance to be tested, to be sure that any contained bacteria are distributed throughout, a small quantity of the fluid is withdrawn with a sterile pipette and transferred to the freshly sterilized fermentation tube. Bacteria present may be slow growers and their presence may not be recognized even after twenty-four hours incubation. The reading should not, therefore, be taken earlier than forty-eight hours after the control culture has been made. Bacterial growth of any kind should be sufficient to cause the material to be withheld.

If the substance under examination is one that may possibly be contaminated by the tetanus bacillus, that is to say, if it is a nutrient fluid or a biological product that has been developed upon nutrient media, or if it is the serum of an animal which might have had tetanus toxin in its blood at the time of bleeding or if in any other way toxic or harmful substances might have gained entrance to it, a cultural test is not sufficient. A quantity, at least relatively equal to the maximum dose that may be used for the patient, should be injected into an animal and the effects of the injection on the animal observed for a sufficient length of time to detect the results of a possible harmful contamination.

Those who have had much experience in the preparation of substances intended for subcutaneous administration, are familiar with the many sources of danger and know of so many instances of serious errors that they are inclined to make too many controls rather than too few. In the larger biological laboratories it is customary to have each product tested in bulk, by two bacteriologists working independently. Products that have passed this test are filled into proper receptacles by means of a carefully sterilized burette or other filling device. Cultural tests are made of the filling device before any filling is done, and a number of filled containers selected at random are examined bacteriologically to be certain the filling has been done properly. In addition to this the special rooms above mentioned are set aside for the filling, and these are given unusual care.

It is evident that if remedies intended for parenteral administration are to be dispensed only after passing through the rigorous tests mentioned above, they must be prepared by persons who have had training in bacteriological *technique*. A realization of this fact is leading the colleges of pharmacy to give their students advanced training in special bacteriological *technique*. To be useful such courses should be thorough. It is apparent that here a little knowledge might be a dangerous thing indeed. Certain criticisms of the tests suggested for the preparation of remedies for parenteral administration will undoubtedly be made. Some persons will say, many others will think, that we have been getting along all these years with much simpler methods—why not continue? The reason we may not continue with them is that these simpler methods are the cause of serious and even fatal infections. We learn of some of them, there are probably ten times as many that we never hear about. The demand for sterile solutions for hypodermic and intravenous injection is destined to increase, these solutions must be sterile and their sterility must, before use, be demonstrated by adequate tests.

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## DISCUSSION.

M. I. Wilbert, of Washington, D. C., said that, from a pharmaceutical point of view, he believed Dr. Hitchens had demonstrated clearly and fully that the only safe and reliable method of sterilization was the very simple one outlined in the German Pharmacopœia: "Sterilization should be done in accordance with established bacteriological *technique*." That was the only safe method of sterilization. It was absolutely unsafe to follow any published prescription or formula. Discontinued sterilization was often spoken of as being absolutely safe, but it was not. In connection with solutions that were themselves antiseptic, like physiological salt solution, if the substance were contaminated by spore-bearing organisms, it could be sterilized half a dozen times, and still be extremely dangerous. Discontinued sterilization depended largely on the development of spores into viable organisms, recognizing that spores themselves are not affected at the ordinary temperatures used. Therefore, ordinary sterilization, unless at very high temperature, would have no effect. Sterilization at high temperatures was not without possible dangers. Repeated work on distilled water had shown that this form of water afforded favorable conditions for the growth of microorganisms; and under certain conditions, as had been shown recently, distilled water might contain, after three or four days, a tremendous number of organisms. The use of such a contaminated water is objectionable from every point of view, even if properly sterilized it would involve risks from generated poisons or the killed organisms themselves.

In connection with the possibilities of the sterilization of local anesthetics, a considerable amount of work had been done in Germany; but the field was so large that there was no end to the possibilities in that direction. Cocaine solutions, that Dr. Hitchens had said could be sterilized at 70 degrees, could also be heated to a considerably higher temperature for a very short time. So that with recently distilled water, and satisfactory conditions so far as containers were concerned, solution of cocaine could be heated to even 100 degrees for a few minutes. Such a solution would be reasonably safe; not absolutely safe, but reasonably so. He said Dr. Hitchens had covered so much ground that it was hard to grasp it all at once, but he hoped the members would fully appreciate his first statement, which was that sterilization should only be successfully done with adequate control, and in strict accordance with bacteriological *technique*.

Chairman Havenhill commented that this certainly was a live subject, or soon would be, with pharmacists. He said he understood the next Pharmacopœia would contain a chapter on sterilization.

E. Fullerton Cook, of Philadelphia, said that one point Dr. Hitchens brought out was worthy of still further emphasis, viz.: that suggestion which made it possible for the phar-

macist to prepare sterile solutions in ampoules with the use of simple apparatus only. He suggests that suitable solutions in non-soluble glass ampoules, may be sterilized after the ampoules are sealed, by placing them in oil or saturated salt solution, and heating for fifteen minutes at a temperature of 115° C. This operation requires only the use of a covered vessel and a thermometer, while the results obtained would approximate those secured through the use of an expensive autoclave; that is, the temperature would be the same as that of the autoclave and the pressure, consequently, inside of each ampoule would be equivalent to the pressure in the autoclave under those conditions.

Such a process is not applicable to all substances, since the temperature required is prohibitive at times, and yet this plan is so simple and where it can be applied so easily and promises such satisfactory results, that it should not be passed over without the emphasis here given.

F. W. Nitardy, of Denver, said his practice was to use steam at 30 pounds pressure in the process of sterilization, keeping it at that point for fifteen minutes. He considered this sufficient sterilization.

Doctor Hitchens, responding to the last speaker, said he thought there was no doubt about the efficiency of this method, provided precautions were taken to have the steam completely replace the air in the chamber. And yet, without control, it would fail. In the ten years he had been doing this work, he had failed many times; but the failure was because somebody had not taken the precaution to remove the air, with the result that the sterilization would not be complete, unless the temperature was raised very high. As he had tried to bring out, and as Mr. Wilbert had kindly emphasized, sterilization must always be controlled by proper cultures. Such cultures are usually made in fermentation-tubes, containing freshly sterilized 2 percent dextrose *bouillon*. With all the precautions ordinarily taken, failure sometimes occurred.

Otto Raubenheimer, of Brooklyn, said he desired to emphasize one point—a thing that should be well known to pharmacists at this time; that distilled water was not necessarily sterile water. Some gentlemen seemed to be of the opinion that sterilization can be attained very easily. But Dr. Hitchens and Mr. Wilbert had properly emphasized the necessity of bacteriological control. He related his observance of a city milk-inspector taking samples of milk for analysis from several milk-wagons, and of the indifference to the exposure of these samples to contamination by bacteria. By the methods pursued by this inspector it must follow that the milk would show excess of bacteria, and he presumed that the milkmen from whom the samples were taken would be disciplined. This incident, he said, would show how carelessly such work is done,—work that should be done with great care and precaution; and all work of sterilization should be guarded with the utmost precaution.

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## METAL COLLOIDS—THEIR INCREASING IMPORTANCE AS REMEDIAL AGENTS.

CHAS. E. VANDERKLEED AND FRITZ HEIDELBERG.

Perhaps no field of chemical and physical research so well shows how rapidly progress is being made, as a glance at some recent developments in the study of colloids, and particularly at the changes that are being made in our conception of colloids. Just as we no longer believe that atoms are actually indivisible—though for all or nearly all of the purposes of the art of chemistry we may still so consider them; just as we no longer are convinced of the absolute indestructibility of matter—though for all practical purposes in chemistry and mechanics we may so calculate; so do we no longer adhere to Graham's original classification of matter into crystalloids and colloids. We may no longer look upon colloids as a distinct class of substances, separate and apart from other classes

of substances, any more than we can consider gases or liquids or solids as distinct subdivisions of matter. Just as many substances may appear in solid, liquid or gaseous form, so may almost, if not indeed all substances, whether or not they possess the power to crystallize, appear under certain conditions as colloids. In the words of Wolfgang Ostwald in his "Grundriss der Kolloidchemie,"—"Unter geeigneten Bedingungen grundsätzlich alle Stoffe in kolloiden Zustand ersheinen können." (Under certain conditions, fundamentally all substances may appear in colloidal form.) Colloidal chemistry may not therefore be defined as the study of colloidal substances, but rather as the study of the colloidal condition of matter.

The authors of this paper will not presume to enter into a discussion or even a review of the recent theoretical developments of colloidal chemistry and physics. Suffice it to say that to the physicist and student of theoretical chemistry, the subject is of utmost importance and interest. Like radio-activity, the study of the colloidal form of matter may prove to be one of the means of bridging over the gap between matter and energy, while biologic and physiologic chemists may ultimately find in the study of colloids the chemical and physical solution of life itself. Many volumes of researches, discourses, and text-books on the subject have appeared, notable among which may be mentioned, Ostwald's "Grundriss der Kolloidchemie"; "Die Kolloide in Biologie und Medizin," by Bechhold; "Kolloidchemie des Lebens," by Liesegang; and a very interesting little book in English entitled, "An Introduction to the Physics and Chemistry of Colloids," by Hatschek. A monthly journal, the "Zeitschrift für Chemie und Industrie der Kolloide," now in its twelfth volume, has recently been supplemented by an "Ergänzung" called "Kolloidchemische Beihefte,"—all devoted to the development of the theory and practical application of colloids. Ostwald expresses the opinion that such problems as the relationship between color, constitution, molecular form, solvents, etc., may ultimately be solved by the study of colloidal forms of matter.

Neither shall we re-state the well-known, and for practical purposes valuable, classifications of colloids by Graham (1861-1864) into "sols" and "gels"—hydrosols, organosols, and hydrogels,—reversible and irreversible, etc. For the purpose of this paper it is sufficient that we picture the colloidal form merely as a state of exceedingly fine subdivision,—so fine indeed that the individual particles closely approach in size, the minuteness of molecules themselves. Colloidal solutions become then merely a fine suspension of one material in another,—and theoretically we should be able to produce any known substance in the form of a colloidal solution. Such so-called solutions differ, however, from true solutions in that the latter are, so far as physical means permit us to determine, absolutely homogeneous, whereas colloidal solutions are, ultimately, only suspensions, even though the highest power of the microscope may not enable us to see the individual particles. In other words, in the case of a true solution we are dealing with a single phase system as we say in physical chemistry, whereas in the case of a colloidal solution, we are dealing with a two-phase system. If the colloidal particles are solids, they are called "suspensoids"; if liquids, they are termed "emulsoids," owing to their occupying intermediate places, respectively between suspensions of solids and emulsions of liquids,—and true solutions.

Permit us to emphasize the fact, however, that there is no chemical difference between matter in or out of the colloidal form. There is no chemical difference between ordinary mercury and colloidal mercury, any more than there is any chemical difference between ice, water, and steam. Each is in a physically different form, yet all three are water from a chemical point of view. Even the distinction that may be drawn between colloidal and non-colloidal forms of matter by the process of dialysis, does not betoken any chemical difference. Sodium chloride in solution dialyzes because there are no particles present larger than the pores of the parchment, but a solution of glue will not dialyze because the particles of glue in pseudo-solution are too large to pass through. If, however, a dialyzer with larger pores be used,—such for example as a thin collodion bag,—or if a colloid with more finely divided particles than those in the glue be used, this colloid will pass through the dialyzer, though not so rapidly as the crystalloid.

We will understand clearly the nature of a colloidal solution if we consider the changes which occur in an ordinary suspension. If we put sand in water, the sand will settle very quickly to the bottom of the container; if we grind the particles of sand finer, they will still settle completely after being suspended for some time in the water; the finer we grind the sand, the longer it will take for the particles to settle. This is due to the fact that the force of gravity which acts on the particles of sand is counteracted in part by several factors like friction in the liquid, molecular attraction, etc.

Let us imagine now that we are able to grind the particles so fine that this counteraction,—viscosity of the water, molecular attraction, the motion akin to the Brownian movement of very small suspended particles, and the electrical charges with which small particles become endowed,—is equal to the force of gravity tending to bring each particle of sand to the bottom of the container. What is the result? The particles no longer, or at least no longer quickly, fall to the bottom, but remain in suspension in the liquid,—and we thus obtain a colloidal solution,—colloidal sand dissolved in water. In the same way, we can imagine the production of a suspension of sand in oil, where by grinding the sand particles finer and finer, we could finally obtain a colloidal solution of sand in oil. A colloid therefore may be not only water-soluble; it may be oil-soluble, or soluble in any other solvent; and it will depend only on how we choose the medium in which we produce the fine particles, whether the finished product will be water-, alcohol-, or oil-soluble, etc.

Actually, we are not able, by mechanical means, to grind the particles of a substance to such a degree of fineness that we can obtain a colloidal solution, and we therefore have to make use of chemical or of physical (as distinguished from merely mechanical) reactions to get these particles fine enough, although should we have a grinder at our disposal to enable us to grind them sufficiently fine, the resulting colloid would probably be just as good as one obtained by chemical means.[1] Thus, while we are not able to grind sand to a state of colloidal fineness by mechanical means, we can readily prepare a colloidal solution of silicic acid

[1] Colloidal filaments of tantalum, tungsten, etc., are made by grinding the metals to an impalpable powder, mechanically, and then treating them alternately with acid and alkali, when they finally assume colloidal form. But the mechanical grinding alone just falls short of producing the desired result.

by chemical and physical means. It is only necessary to decompose a water-solution of sodium silicate with a slight excess of hydrochloric acid and dialyze the mixture until free from excess of acid and sodium chloride, when there will remain in the dialyzer a perfectly clear, colorless solution of silicic acid.

Such a colloidal solution, in common with other inorganic colloids, is very readily thrown out of the solution or "sol" form, however, on addition of electrolytes, the theory being that these serve to disperse the electric charge with which the colloidal particles are endowed, and which, by its power to enable them to repel each other, helps to maintain the "sol" form. When this charge is dispersed, the particles, no longer antagonistic to each other, aggregate, and soon the whole mass of colloid particles either settles out, or as in case of silicic acid, solidifies to a "gel," enclosing by adsorption the water in which it was suspended.

Colloidal solution of ferric hydroxide, or dialyzed iron, is made by a process analogous to that described for silicic acid,—while colloidal solutions of the metals, such as gold, silver, platinum, copper, and lead, are usually prepared by an electrolytic disintegration method first described by Bredig in 1898. This method consists in passing an electric current, in the form of an arc, between poles of the metal which is desired in colloidal solution, the poles being suspended in the desired liquid, usually water. Under this treatment, particles of the electrodes are broken off in such a fine state of subdivision that they remain suspended in the liquid in colloidal form. Here too, however, the addition of electrolytes soon causes the colloidal metal solutions to precipitate as "gels" which cannot be reconverted into solution-form.

A third method of obtaining inorganic colloids is by reduction. If, for example, we take a solution of a metallic salt like gold chloride, and add a diluted solution of formaldehyde, or any other suitable reducing agent, the gold will be reduced and suspended in colloidal solution if the solution be sufficiently diluted. Again, certain colloids may be prepared by oxidation. If we oxidize hydrogen sulphide gas to sulphur by means of sulphurous acid, the sulphur will assume the colloidal form and remain suspended in colloidal solution.

Just a word as to the probable size of these colloidal particles. First of all, they are so small that they cannot be seen in the ordinary microscope, and as Abbe has shown that the lower limit of visibility is from 800 to 400 millionths of a millimeter, while the wave lengths of light lie between 450 and 760 millionths of a millimeter, it follows that these colloidal particles must be much smaller than these wave lengths themselves. Hence they would forever have remained invisible to the naked eye, had not Zsigmondy and Siedentopf invented the ultramicroscope, which by means of the so-called dark-field illumination, only light reflected or dispersed by the particles, and no direct rays from the source of illumination, enter the microscope. In this way particles calculated to be as small as five millionths of a millimeter can be seen. By a study of so-called "ultra-filtration" methods, Bechhold has passed colloidal particles in solution through filters calculated to have pores not greater than 21 millionths of a millimeter in diameter, whence it follows that the particles must have been smaller than these pores and hence have at least approached in smallness the limits which have been assigned from other investigations for the diameter of molecules.

According to Dr. Conrad Amberger,[1] the effect of gravity on colloidal particles in suspension is neutralized by the action of the electrical charges when the particles are not greater than 60 millionths of a millimeter in diameter. Since, however, the addition of an electrolyte serves to disperse this electric charge, no inorganic colloid solution would appear to be sufficiently stable for use, for example, in medicine. Fortunately, however, it was long since discovered that by adding a portion of an organic colloid to an inorganic colloidal solution, preferably prior to the formation of the latter, the inorganic colloid is rendered quite immune to the precipitating action of electrolytes. This is probably best explained by Bechhold's theory that the organic colloid, such as glue, gelatin, casein, albumin, etc., forms a layer around the inorganic colloid particle, and as the organic colloids are but little affected by the addition of electrolytes, precipitation is thus prevented. For this reason organic colloids used in connection with inorganic colloidal solutions to prevent precipitation have received the name "protective colloids."

Thus, there is rendered available for use as therapeutic agents, in relatively stable colloidal solution form, many substances otherwise insoluble. If, however, the colloidal state does not necessarily imply a change in chemical composition, of what possible interest can colloids be in medicine? A consideration of this question brings to light first of all the fact that oftentimes very slight changes in a substance may be the means of materially changing its physiologic effect. Substances of like chemical composition, but differing slightly in the atomic arrangement of their molecules, may differ materially in toxicity and in the effects which they produce. Who shall say therefore that a metal for example, or a metallic oxide or hydroxide or salt in colloidal form, may not differ materially in its potency or in its effect from that of its ordinary form? The question of absorbability, the rapidity with which it may be assimilated, plays an enormous part in treatment with medicinal substances. It is not only conceivable, but highly probable, that this rate of assimilation will be entirely different for mercury, for example, in ordinary globular form, though very finely subdivided mechanically, and mercury many thousands of times more finely subdivided in colloidal form. Hatschek in the closing chapter of his little book says, "The study of colloids shows us that the mere subdivision of matter, or, in other words, *the production of large surfaces,* brings into play energies, the effects of which may be of the most varied character, and of the most profound importance."

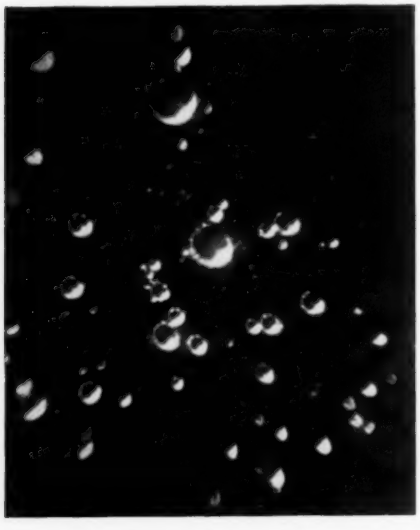
Moreover, the growth of the art of putting into colloidal form and hence making possible the administration of certain substances in solution or liquid form which otherwise could only be administered if at all in solid form,—and then not hypodermically or intravenously but only by mouth or by external application,—shows at once that there is really a promising field for investigation by the therapeutist of a new line of materia medica products made possible by new discoveries in the production of colloidal solutions.

Another evidence of the possible therapeutic activity of colloid metals, is their possession of the power of catalytic action so resembling in many ways the action of enzymes that Bredig has called them "inorganic ferments." Exceedingly

[1] Pharmazeutische Zeitung, *58*, 1913, p. 188.

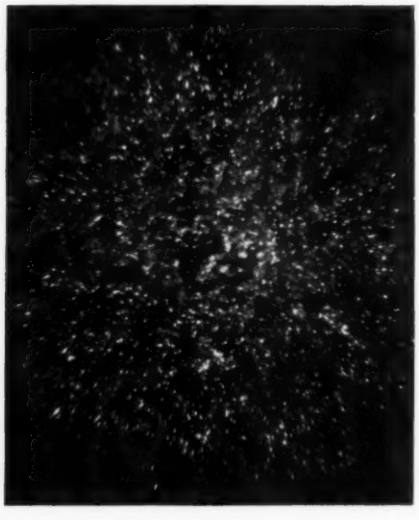
dilute solutions of colloidal platinum and osmium will instantaneously decompose very large quantities of hydrogen peroxide into oxygen and water,—while other colloid metals have been used to polymerize fatty oils into hard masses,—powers not possessed by these metals even when subdivided to the highest possible degree by mechanical means.

Nor have physicians been slow to take up this line of investigation. We refer of course to a study of the therapeutic effects of colloidal solutions of metals, oxides, hydroxides, and salts, which in ordinary form are insoluble in water or in other suitable vehicles for their administration. It is hardly to be conceived that any advantage would ensue from the administration in colloidal form of a substance naturally soluble in a suitable solvent. But there remains a large number of substances, of which the metals and some of the non-metallic elements are



A

Ultra-micro-photograph (x1000) of Blue Ointment U. S. P. dil. to 10%.



B

Ultra-micro-photograph (x1000) of Colloidal Mercury Ointment, 10%.

examples, which, unless made "soluble" by rendering them colloidal, must remain unsuitable for use in the materia medica.

Perhaps the first of metal colloids to be introduced into medicine, colloidal ferric hydroxide, or dialyzed iron, is now acknowledged to be a therapeutic failure,—or at least to possess no advantages that are not to be gained from the administration of iron in other forms. This, however, need not deter us from investigating other colloids, for it must be remembered that dialyzed iron was only administered by mouth, and it is probable that slighter differences will be noted between colloidal and non-colloidal forms when thus administered, than when used hypodermically, intramuscularly, or intravenously.

Among the earliest of the metallic colloids to be employed in medicine was silver,—in the form of pseudo-salts with protein and other organic acids,—colloidal in nature, though tried out and used before many of the investigations of colloids had disclosed their real nature. Of undoubted value in the treatment

of certain bacterial diseases from the clinicians' point of view, these colloidal silver preparations possessed little or no direct bactericidal power,—particularly in comparison with solutions of crystalline silver salts. True, they possessed the advantage, much appreciated by the patients, of being non-irritating,—but of what use is a negative advantage unless accompanied by decided positive advantages? Satisfactory, or at least helpful results, however, were consistently claimed by, not a few, but by very many able practitioners. Some explanation other than the possession of antiseptic power must therefore be sought.

Recent investigations of certain French authors (Pastia,[1] Bossani and Marcelet[2]) have shown that colloid metals influence the opsonic strength of a serum against various bacteria. Bossani and Marcelet think that this influence is not due merely to the colloid nature of the substances, in which case one colloidal metal might act as well as another, but varies with the kind of colloid used.

The experiments of these authors along this line were carried on with the purpose of determining how the action of the leucocytes upon streptococci is influenced by colloidal silver. Experiments were made with animals, men and *in vitro*. The serum used in all the experiments was taken directly before the injection of colloidal silver, one hour after the injection, and 24 hours after the injection.

In the work with rabbits, mixtures were made of serum, a 1 : 3 suspension of a 24-hour *bouillon* culture of streptococcus, washed white corpuscles, and physiological salt solution. These were incubated for 15 minutes at 30°, slides were made, and from the cocci contained in 100 polymorphonuclear leucocytes mixed with serum there was subtracted the number contained in the leucocytes of the control tubes, namely those in salt solution only.

The results showed that in every case the injection of colloidal silver, while causing no increase after one hour, caused a decided increase of phagocytosis after 24 hours.

Experiments upon people were carried out in the same way and showed practically the same results.

To determine whether the colloidal silver influenced the phagocytic power of the leucocytes directly, or increased the opsonic strength of the serum, a number of experiments were made *in vitro*. Increasing dilutions of colloidal silver were mixed with serum in one series, with physiological salt solution in another, and white blood corpuscles were added to both. Slides made from each series were examined.

The results showed that colloidal silver does influence the leucocytes directly, but the colloid can increase the opsonic strength of the leucocytes only in the presence of serum.

Colloidal mercury and colloidal mercurous chloride have also been introduced into medicine, but have not apparently been used very extensively, the former possibly because of the unstable character of the marketed product. Dimond in

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[1] Pastia: La presse medicale 1910.

[2] Bossani and Marcelet: Gazette des Hopitanz 1908.

a recent article[1] speaks of highly satisfactory results from the injection of colloidal mercury and silver solutions in various infectious diseases, particularly in connection with specific vaccine and serum treatments, and attributes the favorable results to increased phagocytosis. Dimond has used metal colloid solutions both "protected" and "unprotected" by the presence of "Schultz-kolloid," and declares that the use of the latter has not been followed in his experience by any loss of therapeutic activity.

Recently renewed interest in colloidal medication has been aroused, first in France by the use of a form of colloidal copper for the treatment of cancer and tumors, and later by Dr. Leo Loeb in St. Louis, who has reported[2] on the experimental use both of colloidal copper solutions prepared electrolytically and used intravenously, and of colloidal copper protected with protein substances. His results have been partially successful, and he closes his article in the May, 1913, number of the Interstate Medical Journal with these words, "It seems to us necessary, in the interest of science and of practical medicine, to follow to the utmost these lines of investigation."

Following the preparation some time ago of a colloidal silver oxide, our research laboratory has been engaged in a study of the production of other colloids. Renewed interest in the use of mercury by intramuscular injection, usually in the form of "Grey Oil" of the British Pharmaceutical Codex, a mechanically subdivided suspension of mercury in liquid petrolatum and lanoline, suggested to us the advisability of preparing a colloidal mercury soluble in oil, thereby possessing the advantage of stability, if not indeed possessing greater therapeutic activity because of the many thousands of times more highly subdivided nature of the mercury particles.

Such a colloidal solution, containing five percent of colloidal mercury, is here shown, together with a specimen of the ordinary "Grey Oil" diluted also to a five percent strength for the purpose of comparison.

An interesting fact was brought out in our experimental work in preparing these colloids, namely, that the solubility of the resulting product, if protected by a so-called "Schutz-kolloid," depends upon the nature of the "Schutz-kolloid" or protective colloid employed. If, for example, metal colloid be protected by means of a caseinate which is water-soluble, the product will dissolve to a clear solution in water, which may be shaken with petroleum or with chloroform without the latter taking up anything from the water solution. On the other hand, if an oil or chloroform-soluble protective colloid, such for example as lanoline, has been used, the product will dissolve to a clear solution in chloroform, which in turn may be shaken with water without loss of any material to the water layer.

This is here shown by two samples of colloidal selenium, one protected by a water-soluble colloid,—the other by an oil-soluble colloid. Selenium has been used in the form of a selenium-eosin compound by Wassermann in the experimental treatment of cancer,—and this metal has ardent advocates who claim therapeutic virtues for it in many forms. These colloidal forms are now being

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[1] The Practitioner XCL July, 1913, p. 132.

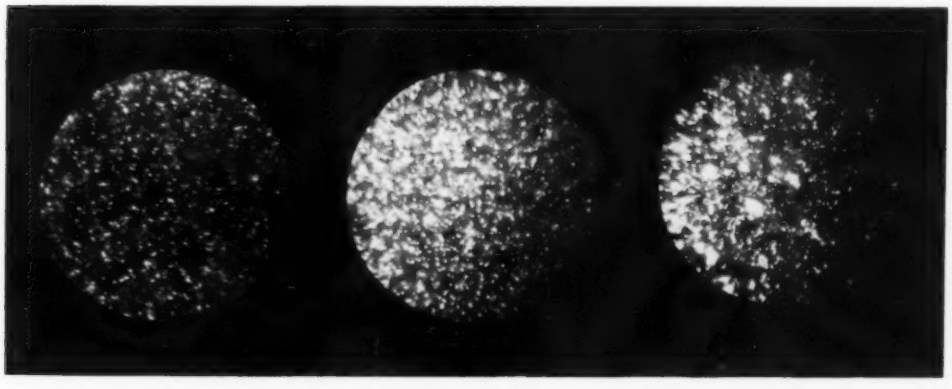
[2] Interstate Medical Journal, 1913.

Journal of the American Medical Association LX, June 14, 1913, p. 1857.

tested experimentally and clinically for their possible value in the treatment of malignant growths.

The production of an oil-soluble colloidal mercury also suggested to us the possible advantage of mercurial ointment in colloidal form. Here is shown such a 10 percent ointment, the vehicle consisting of lanoline and petrolatum, and the whole ointment, mercury and all, being soluble in chloroform, unlike ordinary Blue or Mercurial ointment which, when treated with chloroform, separates into a solution of the vehicle and metallic mercury which settles to the bottom of the tube.

We also show herewith ultra-micro-photographs of ordinary mercurial ointment in comparison with 10 percent colloidal mercurial ointment. These photographs, taken with an enlargement of approximately 1000 diameters by means of a dark-field illuminating apparatus, seem to bear out a calculation, based upon a measurement of the particles in the ordinary ointment and the theoretical size of the colloidal particles, that in amounts of the two ointments containing equal weights of mercury, there is approximately 60,000 times as much mercurial sur-



C

Ultra-micro-photograph (x1000) of Colloidal Mercury Ointment with lowest possible illumination.

D

Same as C, but with increased illumination.

E

Same as C and D, but with more intense illumination.

face exposed in the colloidal ointment as in the ordinary form. In this connection it is of interest to point out, however, that the individual particles in the colloidal ointment, though theoretically magnified only about 1000 diameters in the photograph, are actually many times smaller than this, due to the fact that to the observer, the particles themselves are luminous and sources of light. Consequently, the brighter the illumination (a high power arc is required), the larger the particles will appear. This is well shown in photographs C, D and E, which represent the same colloidal ointment with gradually increasing intensity of illumination. The particles appear to coalesce into luminous nebulæ with increase in luminosity, while if the latter be decreased, the individual character of the particles again becomes discernible. Moreover, no adequate conception of the actual size of the particles can be had, because they are in indescribably rapid motion similar in appearance to the so-called Brownian movement of floating dust particles. Thus each bright spot, as shown particularly well in photograph B, represents not the size of one colloidal particle magnified 1000 times, but rather

the entire circumference of the glow of a particle rapidly vibrating throughout a space very many times its own actual dimensions.

These ointments are also undergoing clinical tests and investigations. It may be of interest, however, to report that the toxicity of colloidal oil-soluble mercury, as determined upon guinea pigs, compared with ordinary metallic mercury appears to be about four times as great. The bactericidal power of water-soluble colloidal mercury has also been determined and appears to be equivalent to a phenol-coefficient of about 27.7.

Here also are samples of water-soluble colloidal copper, protected with casein, and ampoules of the aqueous solution ready for hypodermic or intravenous injection. Each ampoule contains 10 milligrams of substance corresponding to 2 milligrams of metallic copper, this quantity being the mimimum lethal dose for 250 gm. guinea pigs. All these metallic colloids have been produced by the reduction method, starting with soluble salts.

Without doubt many things remain to be learned by the employment of these products in medicine, and the earnest co-operation of careful laboratory and clinical investigators along these lines may lead to discoveries of untold importance in the treatment of disease.

RESEARCH LABORATORY OF H. K. MULFORD COMPANY, July 28, 1913.

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## A PHARMACODYNAMIC STUDY OF THE PITUITARY GLAND WITH TESTS OF A NEW PRODUCT.

FRITZ HEIDELBERG, PAUL S. PITTENGER AND CHARLES E. VANDERKLEED.

The role which the pituitary body or hypophysis plays in life has until recently been a mystery. It was at first thought that its function was to lubricate the nasal cavities. This belief, however, was soon discarded and replaced by the supposition that the gland was, like the appendix, of no use at all. Later, however, it was proven by Vassale and Sacchi,[1] Caselli[2], and others that the gland plays a very important role and is absolutely necessary to life. It has also been found that acromegaly and other diseases are due to functional disturbances produced by an over or an under secretion of this gland, and that its removal causes death. According to Sajous[3] the anterior lobe may prove to be the center of the adrenal system.

The pituitary body varies in size according to the age and species of the animal. The gland most commonly used in therapeutics is that obtained from the ox, and is about $\frac{3}{4}$ inch in diameter.

The gland is composed of two parts or lobes,—the anterior and the posterior or infundibular. The smaller or posterior lobe, which forms only about ten to fifteen percent of the total gland, is the more important therapeutically. This

[1] Vassale and Sacchi: Rivista Sperimentale de Freniatria p. 83, 1894.
[2] Caselli: Studii anatomici e sperimentali sulla Fisiopatologia della Glandola pituitaria, 1900.
[3] Sajous: Internal Secretions and the Principles of Medicine. Vol. 1, p. 216.

lobe contains practically all of the active principles while the anterior lobe is the one which is so necessary to life.

The total pituitary body contains about 80 percent of water, or in other words 100 parts of the fresh gland give about 20 parts of dry substance, containing 2 to 3 parts of the posterior lobe.

Knowledge concerning the chemical composition of the pituitary gland has only recently gained proportions sufficient to warrant the hope that science will ultimately be as successful in isolating and synthesizing its active principle or principles as it has been with the suprarenal gland. Owing to the similarity existing between the physiologic actions of the pituitary and those of the suprarenal gland the theory has been advanced that the active principles of the former will be very similar to epinephrine. In fact it has been shown that the activity of the gland can be concentrated into a basic fraction forming salts with acids. It was possible, however, to split this basic fraction into several fractions of different chemical properties (Fuhner)[4], which would tend to prove that the action of the pituitary body is due to not one but to the combined actions of

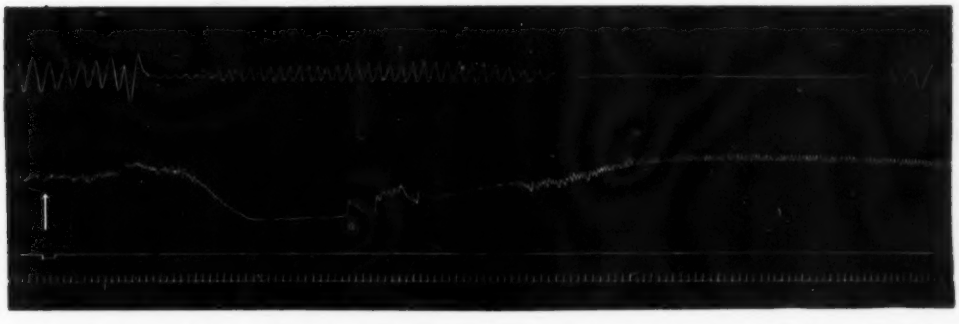

FIGURE 1.—Cut of Prof. Führer's tracing showing the action of the basic fractions, tested by him, on blood pressure (negative).

several active principles. Schäfer and Vincent[5] had also shown sometime before that the blood-pressure-raising principle could be divided into two fractions by their different solubilities in alcohol, one containing a pressor and the other a depressor action.

Practically all of the commercial preparations of pituitary on the market are claimed to be extracts of only the posterior lobe. Since the process of separating the posterior from the anterior lobe is both very tedious and expensive, the object of our endeavors has been to isolate from an extract of the whole gland, either a highly active fraction or the active principles themselves. We have also been concerned in endeavoring to differentiate between extracts or solutions claimed to be prepared from certain portions of the gland, and those from the gland as a whole, as we doubt very much whether, in all cases, preparations said to be made from the posterior portion are really not prepared from the gland as a whole.

Physiologic experiments have demonstrated that extracts of this gland are

[4] Fuhner: Hypophyse deutschen medizinsche Wochenschrift, March, 1913, p. 491.

[5] Schäfer and Vincent: Journal of Physiology, May 11, 1899.

valuable therapeutic agents. Thus Magnus and Schäfer[6] and Schäfer and Herring[7] have shown that it accelerates diuresis; Oliver and Shäfer[8] that it is valuable for raising the blood pressure by arterial constriction; Dale[9], Bell and Hicks[10], and v. Fränkl Hochwart and Frohlich[11] that it excited marked uterine contractions, Ott and Scott[12] that it possesses a rather marked galactagogue action.

The scant knowledge of the chemical composition of the gland and extracts of the same, renders it impossible to ascertain by chemical means the comparative value of two or more extracts or fractions. We are therefore compelled to resort to physiologic assay methods. Of the various physiologic actions of the gland above mentioned there are three which present themselves as possible means of

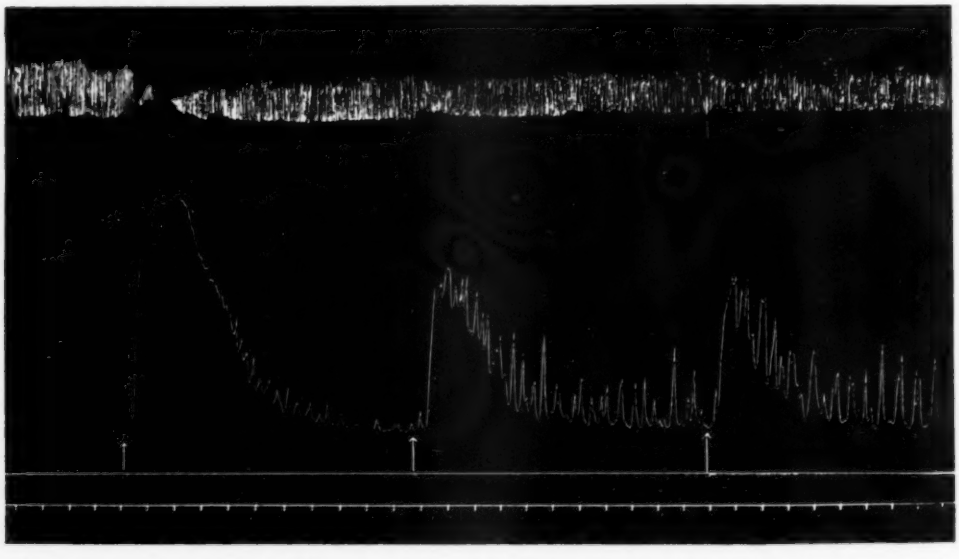

FIGURE 2.—Cut of Prof. Führer's tracing showing marked uterine contractions produced by the same preparation which gave negative results by the blood pressure method (See Figure 1).

physiologic standardization, i. e., the action of the blood pressure, the uterus, and the kidneys.

The fact that the blood-pressure method involves the simplest *technique* together with its satisfactory and almost universal use as a means of standardizing epinephrine and suprarenal extracts would at first lead one to believe that this method would also be the most satisfactory one for standardizing pituitary extracts. It has, however, serious disadvantages in case of the latter. As before stated, the blood-pressure-raising principle can be divided into two parts, one

[6] Magnus and Schäfer: Proc. Phys. Soc., p. IX, 1901.
[7] Schäfer and Herring: Phil. Trans., 1906 B.
[8] Oliver and Schäfer: Journ., of Phys., XVIII, p. 277, 1895.
[9] Dale: Biochem. Journ., IV, p. 427, 1909.
[10] Bell and Hick: Brit. Med. Journ., i. p. 777, 1909.
[11] v. Fränkl Hochwart and Fröhlich: Arch. f. exp. Pathol., u. Therapie, LVII, p. 347, 1910.
[12] Ott and Scott: Proc. Soc. exp. Biol., New York, 1910.

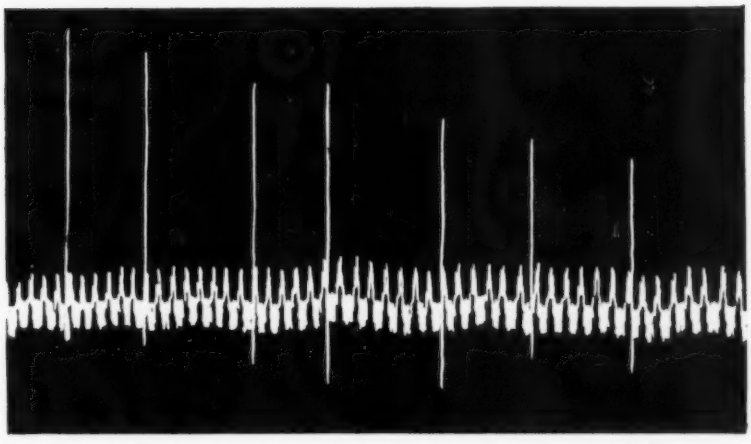

FIGURE 3.—Shows the gradual decrease in the rises in blood pressure produced by repeated injections of equal sizes.

possessing a pressor and the other a depressor action. Prof. Führer of Frieburg[13] has also shown that the sum of the basic principles tested by him caused marked uterine contractions and only a slight pressor action, which was almost completely masked by a marked preliminary depressor action.

Furthermore, extracts which had been deprived of their depressor action by fractionation with alcohol, showed marked pressor effects, while on the other hand they were sometimes almost entirely free from action upon the uterus.

Another serious drawback to the blood-pressure-raising method, is the fact that the active principles of pituitary extract are not nearly as rapidly oxidized as those of the suprarenal gland and therefore repeated injections of equal sizes produce unequal rises,—the subsequent ones generally showing a waning of the pressor action and an increasing prominence of the preliminary depressions.

Still another objection to the blood pressure method is its comparatively low

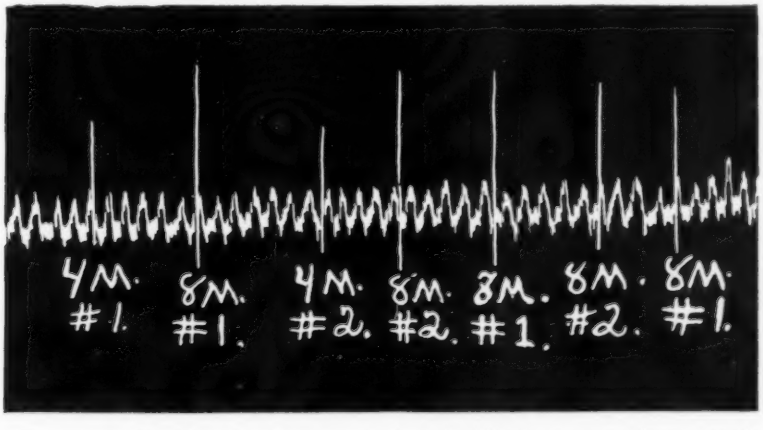


FIGURE 4.—Tracing showing equal rises in blood pressure from equal amounts of the two extracts mentioned above.

[13] Hypophyse deutschen medizinische Wochenschrift 1913, No. 11, p. 491.

sensitiveness; in other words, it requires, in most cases, a rather large variation in the size of the injection to produce a variation in the resultant rise. This latter objection is especially serious when comparing two or more samples for research purposes, in which case a mistake of 20 to 30 percent in interpreting the results of an assay may cause a considerable loss of time. For example, we had occasion during our experiments to compare two extracts made by different processes, in order to determine which was the better of the two. According to the blood-pressure method both extracts showed the same activity, while when

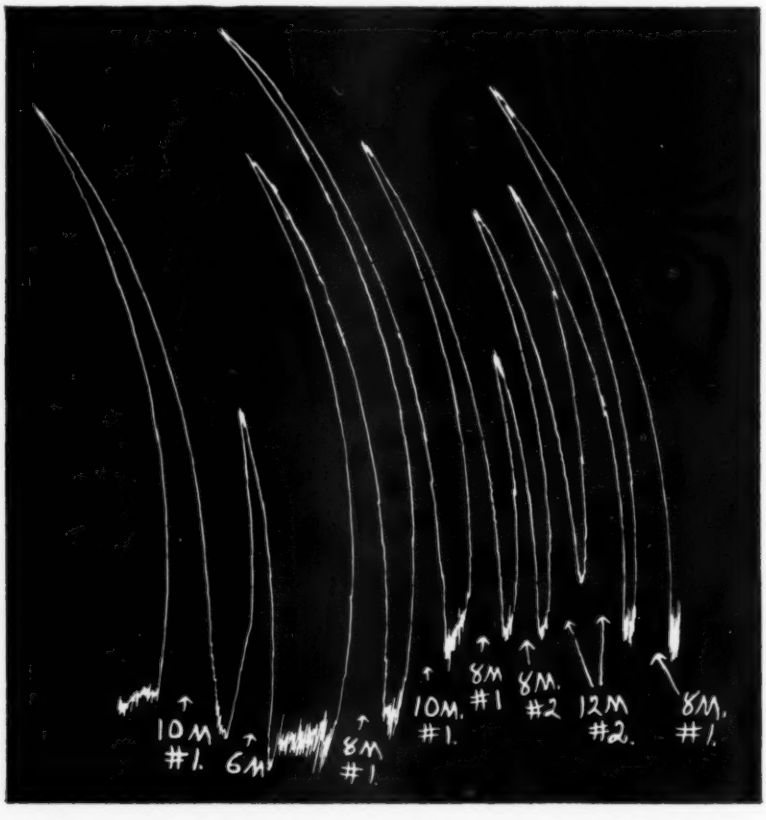


FIGURE 5.—Tracing proving the sensitiveness of the uterine method. Chart shows 8 minims of extract No. 1 to be stronger than 12 minims of extract No. 2. By the blood pressure method (owing to its lower sensitiveness) both preparations showed the same activity (See Figure 4).

tested by the uterine method, which is far more sensitive, 8 minims of one extract prove to be more active than 12 minims of the other. (See Figures 4 and 5).

We have had no experience with methods of standardization based upon the diuretic action, but it has been shown by Dale and Laidlaw[1] that this method is also unsatisfactory, due to the tolerance produced by the first injection. They

[1] "A Method of Standardizing Pituitary (infundibular) Extracts," by Dale and Laidlaw. Journ. Pharm. and Exp. Ther., Sept., 1912, p. 75.

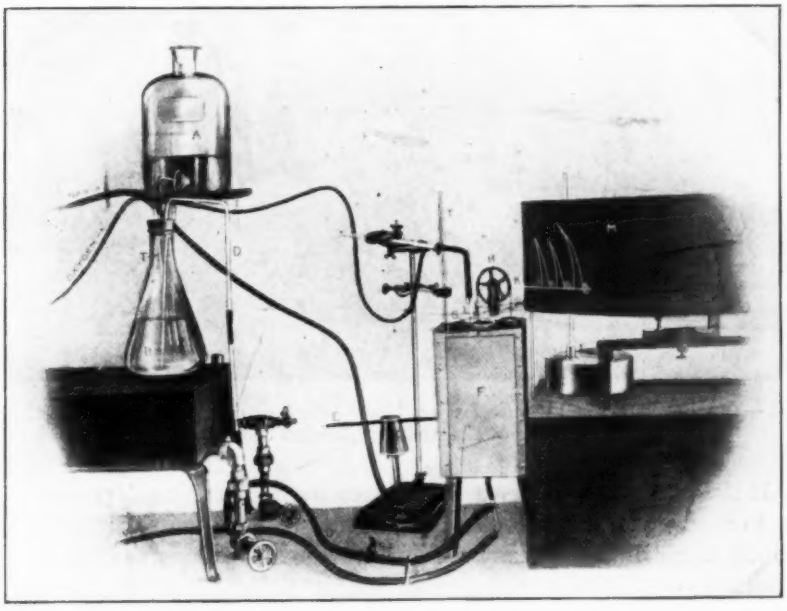

FIGURE 6.—Apparatus employed for testing ergot and pituitary extracts upon the isolated uterus of virgin guinea pigs.

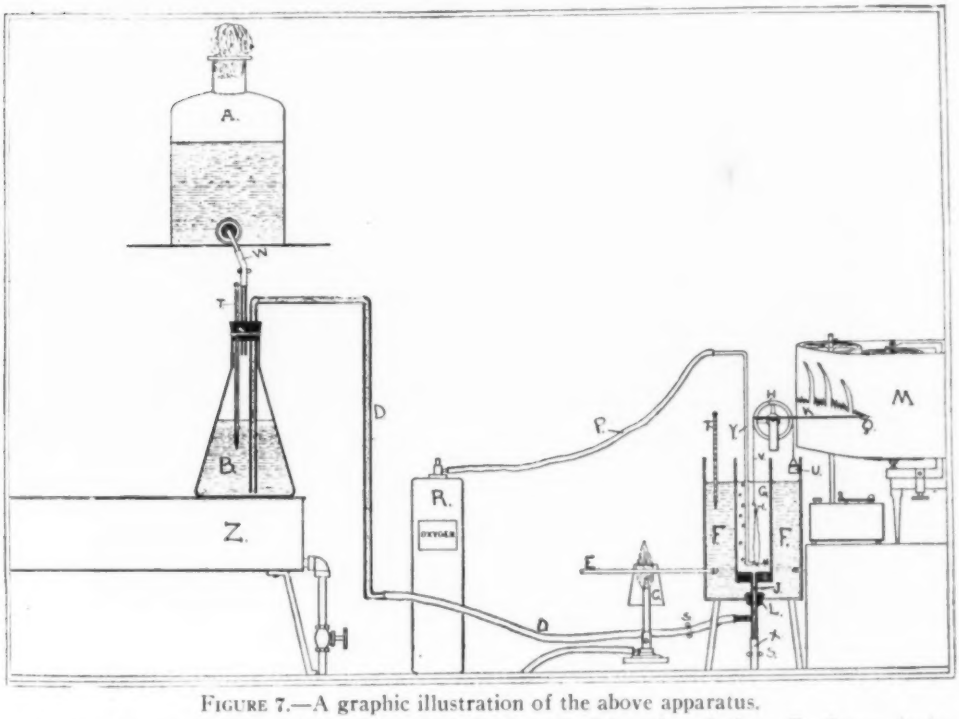


FIGURE 7.—A graphic illustration of the above apparatus.

A—Aspirator bottle containing Ringer's solution; B—Ringer's solution; Z—Steam bath; D—Syphon tube carrying Ringer's solution to cylindrical vessel; F—Constant temperature bath; E—Brass rod; C—Bunsen burner; G & N—Hooks suspending uterus; O—Rubber stopper; X—Tube leading to waste pipe; U—Counter balancing bucket; H—Escapement wheel; K—Writing lever; Q—Writing point; M—Kymograph; T—Thermometers.

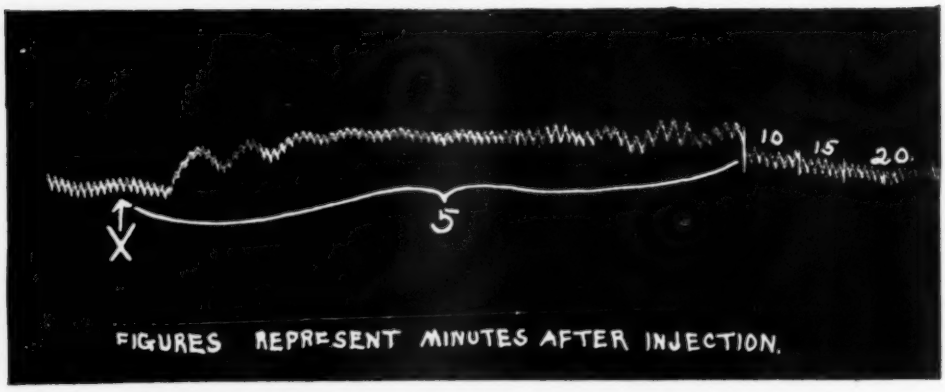


FIGURE 8.—Tracing showing the effect upon blood pressure of intravenous injections of our metallic derivative of the active principles of the whole gland.

state that if small doses are used in order to overcome this tolerance "it may be difficult to distinguish genuine effects from the spontaneous variations of urinary flow which occur in almost any experiment, however constant the controllable conditions."

In our experiments upon the isolated uterus we carried out essentially the method of Dale and Laidlaw with a few modifications of the apparatus employed. We used the same apparatus that we employed in our researches upon ergot, as set forth in another paper[2].

We have used both the uterine and the blood pressure method, during the

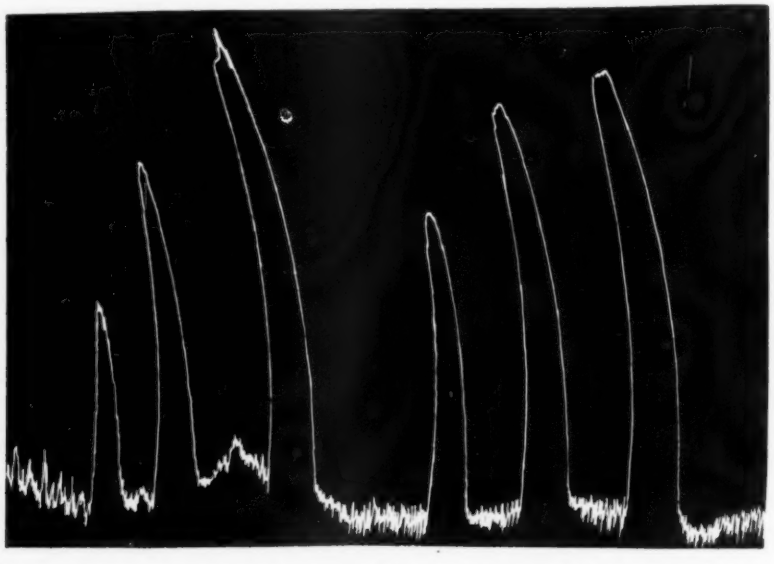

FIGURE 9.—Tracing showing the effect of our metallic derivative of the active principles of the whole gland upon the isolated uterus of the virgin guinea pig.

[2] "A New Uterus Contraction Method of Testing Ergot,—with comparison with the blood pressure method," by Pittenger and Vanderkleed.

past year, throughout all our researches on pituitary substances, and are thoroughly convinced that the uterine method is by far the better of the two. We will not go into a detailed description of the advantages of the uterine method, as our results agree in every instance with the claims made for it by Dale and Laidlaw.

In our experimental work on pituitary extract, we have succeeded in preparing colorless extracts of the *whole gland,* possessing all of the characteristic physiologic properties of the posterior lobe. Such a solution, in sterile ampul form, is here shown, together with tracings, showing the characteristic blood-pressure-raising power, and also the uterus-contracting power, peculiar to the posterior lobe, to a marked degree.

This solution has been prepared as follows: First a watery extract is made of the whole gland. This is then purified by a series of precipitations which deprive the extract of practically all inert proteid substances. This purified extract is then treated with metallic salts of aluminum (or other suitable metals), after which it is neutralized, thus precipitating the metallic derivative. This precipitate is then filtered off, washed, and dried. An aqueous solution of this dried material forms the solution exhibited in the ampoules. The product, therefore, is in reality a solution of a metallic derivative or derivatives of the active principles, in the purification of which, the presence of the relatively inert anterior lobe seems not to interfere, thus permitting of a great saving in the labor and resultant expense of separating the lobes.

We have not yet been able to determine exactly the nature of these metallic derivatives, but are continuing our researches and will give more detailed accounts of further experiments in subsequent papers.

RESEARCH LABORATORY OF H. K. MULFORD COMPANY, August 13, 1913.

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## VARIATION IN SUSCEPTIBILITY OF THE GUINEA PIG.

(Continuation of a previously reported study.)*

CHAS. E. VANDERKLEED, PHAR. D., AND PAUL S. PITTENGER, PHAR. D.

In a paper read at the 1912 meeting of the American Pharmaceutical Association in Denver, the results of a series of experiments covering one year were given, in which it was shown that the average minimum lethal dose of crystallized strophanthin, Thoms, (ouabain) for 250 gm. guinea pigs, varied during the course of the year from 0.0000511 gm. in September, 1911, to 0.0000844 gm. in May, 1912, the average for the year being 0.0000661, and the extreme variation ranging from 22.7 percent below to 27.7 percent above this average. These experiments having conclusively shown that sex and weight may be dismissed as unimportant, this conclusion having been fully concurred in by other investi-

* Variation in the Susceptibility of the Guinea Pig to the Heart Tonic Group, (Second Paper), by Chas. E. Vanderkleed, Phar. D., and Paul S. Pittenger, Phar. D., Journal of the American Pharmaceutical Association, II, May, 1913, p. 558.

gators,** these factors were eliminated in extending our observations over a number of months during the past year, the results of which are given in the following tables. The doses are in all cases those given per 250 gm. weight.

AUGUST, 1912.

Temperature of Laboratory, 29 to 30° C. Aver., 29.5° C.
Temperature of Guinea Pig Quarters, 28 to 29° C. Aver., 28.5° C.
Pigs varied in weight from 220 to 430 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000045..... | — | Recovered | 0.000060..... | + | Died |
| 0.000050..... | — | Recovered | 0.000065..... | + | Died |
| 0.000055..... | — | Recovered | 0.0000675..... | + | Died |
| 0.000055..... | — | Recovered | 0.000070..... | + | Died |
| x0.000060..... | + | Died | | | |

M. L. D. = 0.000060

OCTOBER, 1912.

Temperature of Laboratory, 21 to 27° C. Aver., 24° C.
Temperature of Guinea Pig Quarters, 10 to 16° C. Aver., 13° C.
Pigs varied in weight from 240 to 655 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000050..... | — | Recovered | 0.0000575..... | — | Recovered |
| 0.000050..... | + | Died* | 0.0000575..... | — | Recovered |
| 0.0000525..... | + | Died* | x0.000060..... | + | Died |
| 0.0000525..... | — | Recovered | 0.000060..... | + | Died |
| 0.000055..... | — | Recovered | 0.000060..... | + | Died |
| 0.000055..... | — | Recovered | 0.0000625..... | + | Died |
| 0.000055..... | + | Died* | | | |

M. L. D. = 0.000060

* Died "out of order."

NOVEMBER, 1912.

Temperature of Laboratory, 16 to 22° C. Aver., 19° C.
Temperature of Guinea Pig Quarters, 12 to 18° C. Aver., 15° C.
Pigs Varied in weight from 250 to 505 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000050..... | — | Recovered | 0.0000725..... | — | Recovered |
| 0.000060..... | — | Recovered | x0.0000725..... | + | Died |
| 0.000065..... | — | Recovered | 0.0000725..... | + | Died |
| 0.000065..... | — | Recovered | 0.000075..... | + | Died |
| 0.000070..... | + | Died* | 0.000075..... | — | Recovered* |
| 0.000070..... | — | Recovered | 0.000080..... | + | Died |
| 0.000070..... | — | Recovered | 0.0000825..... | + | Died |

M. L. D. = 0.0000725

* Died or recovered "out of order."

DECEMBER, 1912.

Temperature of Laboratory, 18 to 20° C. Aver., 19° C.
Temperature of Guinea Pig Quarters, 12 to 17° C. Aver., 14.5° C.
Pigs varied in weight from 230 to 410 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000050..... | — | Recovered | 0.0000725..... | — | Recovered |
| 0.000060..... | — | Recovered | x0.0000725..... | + | Died |
| 0.000065..... | — | Recovered | 0.0000725..... | + | Died |
| 0.000065..... | — | Recovered | 0.000075..... | + | Died |
| 0.000070..... | — | Recovered | 0.000075..... | + | Died |
| 0.000070..... | — | Recovered | 0.000075..... | + | Died |

M. L. D. = 0.0000725

** Seasonal Variations in the Resistance of Guinea Pigs to Poisoning, by C. C. Haskell, A. B., M. D., American Journal of Pharmacy, June, 1912, p. 241-246.

JANUARY, 1913.

Temperature of Laboratory, 19 to 21° C. Aver., 20° C.
Temperature of Guinea Pig Quarters, 17 to 19° C. Aver., 18° C.
Pigs varied in weight from 375 to 575 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000060..... | — | Recovered | x0.000065..... | + | Died |
| 0.000060..... | — | Recovered | 0.000065..... | + | Died |
| 0.0000625..... | — | Recovered | 0.000070..... | + | Died |
| 0.0000625..... | — | Recovered | 0.000075..... | + | Died |
| 0.0000625..... | + | Died | | | |

M. L. D. = 0.000065

FEBRUARY, 1913.

Temperature of Laboratory, 18 to 21° C. Aver., 19.5° C.
Temperature of Guinea Pig Quarters, 9 to 18° C. Aver., 13.5° C.
Pigs varied in weight from 200 to 290 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000030..... | — | Recovered | 0.000060..... | + | Died* |
| 0.000040..... | — | Recovered | 0.000065..... | — | Recovered |
| 0.000040..... | — | Recovered | 0.000065..... | — | Recovered |
| 0.000045..... | — | Recovered | 0.000065..... | — | Recovered |
| 0.000050..... | — | Recovered | 0.0000675..... | — | Recovered |
| 0.000050..... | — | Recovered | x0.000070..... | + | Died |
| 0.000050..... | — | Recovered | 0.000070..... | + | Died |
| 0.000050..... | + | Died* | 0.000070..... | + | Died |
| 0.000060..... | — | Recovered | 0.000080..... | + | Died |
| 0.000060..... | — | Recovered | 0.000085..... | + | Died |
| 0.000060..... | — | Recovered | | | |

M. L. D. = 0.000070

* Died "out of order."

MAY, 1913.

Temperature of Laboratory, 22 to 30° C. Aver., 26° C.
Temperature of Guinea Pig Quarters, 22 to 28° C. Aver., 25° C.
Pigs varied in weight from 305 to 520 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000050..... | — | Recovered | 0.000065..... | — | Recovered |
| 0.000055..... | — | Recovered | 0.000070..... | — | Recovered |
| 0.000055..... | — | Recovered | 0.000070..... | — | Recovered |
| 0.000060..... | — | Recovered | 0.000070..... | — | Recovered |
| 0.000060..... | — | Recovered | x0.0000725..... | + | Died |
| 0.000060..... | + | Died* | 0.0000725..... | + | Died |
| 0.000065..... | — | Recovered | 0.000075..... | + | Died |
| 0.000065..... | + | Died* | | | |

M. L. D. = 0.0000725

* Died "out of order."

JULY, 1913.

Temperature of Laboratory, 28 to 31° C. Aver., 29.5° C.
Temperature of Guinea Pig Quarters, 29 to 32° C. Aver., 30.5° C.
Pigs varied in weight from 275 to 520 gms.

| *Dose.* | | *Results.* | *Dose.* | | *Results.* |
|---|---|---|---|---|---|
| 0.000050..... | — | Recovered | 0.000065..... | + | Died |
| 0.000055..... | — | Recovered | 0.000070..... | + | Died |
| 0.000060..... | — | Recovered | 0.0000725..... | + | Died |
| 0.000060..... | — | Recovered | 0.000075..... | + | Died |
| 0.000060..... | + | Died | 0.000080..... | + | Died |
| x0.000065..... | + | Died | | | |

M. L. D. = 0.000065

In order that these results may be considered in conjunction with those obtained during the previous year, the following tabulated summary includes the results reported in the previous paper:

MINIMUM LETHAL DOSE BY MONTHS.

| *Date.* | *Lab.* | *Pens.* | *M. L. D.* | |
|---|---|---|---|---|
| July, 1911 | 27°C. | ..... | 0.0000519 | |
| August, 1911 | 27°C. | ..... | 0.0000519 | |
| September, 1911 | 23.5°C. | ..... | 0.0000511 | |
| October, 1911 | 21.2°C. | ..... | 0.0000544 | |
| November, 1911 | 22°C. | ..... | 0.0000577 | |
| December, 1911 | 18.5°C. | ..... | 0.0000700 | |
| January, 1912 | 20°C. | 12°C. | 0.0000658 | |
| February, 1912 | 18.5°C. | 12°C. | 0.0000737 | |
| March, 1912 | 20°C. | 12.5°C. | 0.0000825 | Old |
| April, 1912 | 24°C. | 17°C. | 0.0000800 | series |
| May-June, 1912 | 25.7°C. | 25.5°C. | 0.0000844 | Aver. |
| July, 1912 | 28°C. | 25.5°C. | 0.0000700 | 0.0000661 |
| August, 1912 | 29.5°C. | 28.5°C. | 0.0000600 | |
| October, 1912 | 24°C. | 13°C. | 0.0000600 | |
| November, 1912 | 19°C. | 15°C. | 0.0000725 | |
| December, 1912 | 19°C. | 14.5°C. | 0.0000725 | |
| January, 1913 | 20°C. | 18°C. | 0.0000650 | New |
| February, 1913 | 19.5°C. | 13.5°C. | 0.0000700 | series |
| May, 1913 | 26°C. | 25°C. | 0.0000725 | Aver. |
| July, 1913 | 29.5°C. | 30.5°C. | 0.0000650 | 0.0000672 |
| Average for two years | | | 0.0000665 | |

A study of this table shows that it is not necessary for us to make any changes in our conclusions of last year's paper. The average M. L. D. for 1911-1912 was 0.0000661 gm.; that for the new series of 1912-1913 was 0.0000672 gm.; while the average for the whole two years was 0.0000665 gm. On the other hand the extreme variations during the new series have been much smaller than those observed during the first twelve months, varying from only 9.8 percent below to 9 percent above, instead of from 22.7 percent below to 27.7 percent above. With less than a 10 percent variation in susceptibility above or below the average, with less than 10 percent of pigs dying or recovering "out of order," we contend that for all practical purposes, the guinea-pig method affords the simplest and most satisfactory means of standardizing the heart tonic group of drugs, at a very reasonably economical cost, without the necessity for standardizing the test animals, and without need for considering seasonal variations. As for the opinion which has been occasionally advanced, that experiments on ouabain really prove nothing as to the possible variation in susceptibility to digitalis or other members of the heart tonic group, we can only say that it would be very difficult to carry out a series of experiments such as we have done, with digitalis, strophanthus or any other drug as a whole. Any variation that might be noted would always cause the question to arise as to possible change in the test material. We can say, however, that in our long experience with this method as a routine one for testing all of the heart tonic drugs, we have found no evidence of any appreciable variation. Moreover, as the physiologic action

of the various heart tonic drugs is very much the same, it is not likely that much variation in susceptibility will be noted. As our opportunities to observe possible variations in the case of vacuum-preserved preparations of digitalis and strophanthus accumulate, we should be able within a year or two more to throw some direct light on this question.

PHYSIOLOGIC LABORATORY OF H. K. MULFORD COMPANY, July 27, 1913.

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## THE YEAR BOOK OF THE ASSOCIATION.*

Fresh from the hands of the printers comes the first year book of the Association, and, with all modesty, it must be said that it reflects the greatest credit upon the Association and upon all of those by whose painstaking efforts the publication makes such a creditable showing; particularly upon its Editor-in-Chief, our esteemed fellow-member, C. Lewis Diehl, Ph. M. and the General Secretary, Dr. James H. Beal, under whose capable direction the publication has been compiled and printed.

The volume is a distinct addition to pharmaceutical literature, not alone of this country, but of the entire world. Nowhere else can be found so completely and so well, within the limits of a single volume, such an infinite amount of valuable material to the profession, as is comprised in this volume of 621 pages. No pharmacist, who has the true interest of his guild at heart, and who desires to keep "in touch" as to its scientific and its practical progress, can fail to find in this "Year Book," matter not only of the greatest interest, but also much valuable information of distinct and immediate profit. Its value to every pharmacist cannot be stated, except in the most general way;—that there is no druggist but will find in its pages something that he can coin into profit, which will many, many times far exceed the trifling cost of the publication to him, personally. It stands as a conspicuous instance of one of the great advantages of the co-operative work which the American Pharmaceutical Association has done and is still doing for every member of the profession. It is a complete and a perfect answer to the criticism, often expressed by the uninformed, that the A. Ph. A. is ultra-scientific, not practical, etc. In the hands of every pharmacist who reads it and who takes advantage of the information packed into its pages, it will be a most useful,—a most valuable,—aid to him in the conduct of his daily affairs, and studied diligently it will make of him a wiser, better and a higher-class pharmacist and man.

In its typography and general make-up it shows the admirable workmanship, care and capacity of the Stoneman Press of Columbus, with which the readers of the JOURNAL are already so familiar. E. C. M.

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*THE YEAR BOOK OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1912, containing the Fifty-fifth Annual Report on the Progress of Pharmacy, and the Constitution, By-Laws and Roll of Members; corresponding to Volume 60 of the former Proceedings of the American Pharmaceutical Association. Published by the American Pharmaceutical Association, 1914, Scio, Ohio.

# Section on Historical Pharmacy

Papers Presented at the Sixty-First Annual Convention

## THE TABLET INDUSTRY—ITS EVOLUTION AND PRESENT STATUS—THE COMPOSITION OF TABLETS AND METHODS OF ANALYSIS.[1]

L. F. KEBLER, PH. C., M. D.[2]

### INTRODUCTION.

It is commonly estimated that from one-fourth to one-third of all the medicaments in the United States are administered in the form of tablets. Considering the comparatively recent origin of the medicinal tablet, there must be unusual reasons for such a phenomenal growth of the industry. Some of the chief merits claimed for this form of medication, are accuracy, elegance, economy, stability, portability, concentration, rapid solubility, absence of alcohol, comparative safety to the consumer, and convenience for the dispensing physician. If it be correct that machinery, appliances, and manual skill have reached a stage of development whereby it is possible to produce tablets having even a part of such a host of virtues, it would seem reasonable to expect that a very large portion of those found upon the market, should possess the composition claimed for them. It was, therefore, but natural that they should be carefully investigated by the Drug Division. A large number of assorted uncoated tablets, purchased directly and indirectly from manufacturers, were examined. The result did not thoroughly corroborate the general view as to uniformity of composition. Various manufacturers were invited to explain the shortcomings. In some instances they were traced to carelessness on the part of the tablet-machine operator, and in others to ignorance of fundamental conditions, loose methods, uncontrolled conditions, chemical, mechanical, and others, which may all be summed up as a failure to realize the necessity of carefully controlling all steps from the selection of the initial ingredients used in the manufacture of the tablet, to the final chemical examination of the finished product. All these, however, did not yet seem to explain the conditions found in some goods known to be prepared under careful control.

In order to obtain first-hand and full information of the industry, the literature on the subject was fully reviewed, laboratory methods, mechanical, supervisory, and analytical, and other elements were carefully studied throughout the United States. Numerous samples were collected and analyzed. This paper, which embodies the results of this work, covers uncoated tablets only.

[1] The historical portion was read before the Historical Section, and the remainder before the Scientific Section of the American Pharmaceutical Association meeting, held at Nashville in 1913.

[2] Chief, Drug Division, Bureau of Chemistry, U. S. Department of Agriculture.

HISTORICAL REVIEW OF THE INDUSTRY.

A review of the history of tablet making shows that the two general methods of manufacture, compression and molding, have had somewhat different lines of evolution. In the first method the powdered medicament was given form and compactness by subjecting it to compression in a suitable hand or power press without the addition of any foreign substance to give adhesiveness or bulk, and only substances adapted for compression in this way were employed. Gradually, however, as tablets grew in favor as a mode of administering medicines, it became desirable to compress other drugs, and it was then found necessary to add excipients, to give the ingredients sufficient bulk or adhesiveness, so that at present, while some compressed tablets contain medicaments only, most of those upon the market contain both medicaments and excipients.

In preparing molded tablets, the active drug is usually first mixed with sugar of milk, the mixture made into a suitable mass with liquid, and the paste pressed into molds from which it is subsequently ejected in the form of tablets. Tablets made in this way are usually designated as tablet triturates, but the distinction between them and the compressed tablets, in so far as it depends upon the method of manufacture, has been gradually disappearing, and the tendency is still in that direction.

From this it will readily be seen that there is at present but little real difference between the two processes so far as the essential details are concerned. Some form of adhesive, excipient or lubricant, and some degree of pressure must be used in both cases. These two processes, as well as the resulting products, such as compressed tablets, molded tablets, tablet triturates, hypodermic tablets, dispensary tablets, dosimetric tablets, veterinary tablets, opthalmic tablets, tablet saturates, etc., will be considered in detail in the following pages.

COMPRESSED TABLETS.

Joseph R. Wood, in his book on tablet manufacture,[3] gives the following footnote:

"Stamps have been found in England which have been shown to have been used by the Romans to stamp remedies for producing clearness of vision, or for doing away with dimness of sight. The object aimed at by the medicament was specified in the stamp. It is noteworthy that the stamps so far discovered were designed for remedies for ocular diseases. The preparations were hardened with gum or some viscid substance and were thus ready to be liquefied at any time. Thus our supposedly very modern device of triturates or compressed tablets is only a revival of an ancient Roman custom."—(*American Medicine.*)

Careful search on the part of the author and of the publisher of "American Medicine" failed to locate this statement. Its authenticity could not, therefore, be verified. Lozenges, troches, and pastilles, however, are referred to by a number of early writers.[4]

[3] Tablet Manufacture, Its History, Pharmacy and Practice, 1906, p. 9.

[4] Hippocrates (460-375 B. C.), Liber prior de morbis mulierum, Mauricio Cordaeo, Rhemo, interprete et explicatore, Karisiis, 1585, pp. 198, 286.

Celsus, A. Cornelius (lived first century, A. D.), De Medicina, Alex. Lee's translation of Targa's edition, 1831, Lib. v, Cap. xvii, p. 14; Cap. xx, p. 35.

Cordi, Valerii, Dispensatorium, sive Pharmacorum, Conficiendorum Ratio. Lugduni Patavorum, ex-officina, Joannis Maire, 1651, pp. 253-279, 515.

Dispensatory of the Royal College of Physicians, London, 3rd ed., 1751, H. Pemberton, M. D., pp. 318-322.

Dispensatorium Pharmaceuticum Universale, etc., Daniele Wilhelmo Trillero, 1764, pp. 791-803.

There is no question that the molding of medicaments was in vogue many years before William Brockedon was granted English Patent No. 9977, December 8, 1843, under the title of "Shaping Pills, Lozenges and Black Lead by Pressure in Dies," and it is equally certain that this invention was the beginning of a great industry. On account of its historical value those portions of the patent and its accompanying illustrations dealing with medicated compressions are here given:

"To all to whom these presents shall come, I, William Brockedon, of Devonshire Street, Queen Square, in the County of Middlesex, Gentleman, send greeting.

"Whereas, Her present most Excellent Majesty Queen Victoria, by Her Letters Patent under the Great Seal of Great Britain, bearing date at Westminster, the eighth day of December, in the seventh year of Her reign, did, for Herself, Her heirs and successors, give and grant unto me, the said William Brockedon, Her special license, full power, sole privilege and authority, that I, the said William Brockedon, my exors, admors, and assigns, or such others as I, the said William Brockedon, my exors, admors, or assigns, should at any time agree with, and no others, from time to time and at all time during the term of years therein expressed, should and lawfully might make, use, exercise and vend, within England, Wales, and the town of Berwick-upon-Tweed, and in the Islands of Jersey, Guernsey, Alderney, Sark and Man, and in all Her said Majesty's Colonies and Plantations abroad, my invention of "Improvements in the Manufacture of Pills and Medicated Lozenges, and in Preparing or Treating Black Lead"; in which said Letters Patent is contained a proviso, that I, the said William Brockedon, shall cause a particular description of the nature of my said invention, and in what manner the same is to be performed, to be inrolled in Her said Majesty's High Court of Chancery within six calendar months next and immediately after the date of the said in part recited Letters Patent, as in and by the same, reference being thereupto had, will more fully and at large appear."

* * * * * * * * * *

"It is well known that in making pills, and also medicated lozenges, as heretofore practised, the proper materials are mixed with a suitable liquid into a state of stiff paste, which is divided and shaped and allowed to dry, and it is well known that in some cases the gum and other materials, used as adhesive matter for keeping pills and lozenges in form, when the same are mixed by means of fluids, interfere with and prejudice the desired action of the matters employed in making up or preparing pills and lozenges, and these gums and adhesive matters are rendered necessary by the use of fluids for getting the matters into a condition to be shaped. * * * * * *"

DESCRIPTION.

"Figure 1 shows the section of suitable dies for making pills, and similar dies will be used when making medicated lozenges, but the same would be formed into suitable figures to produce lozenges of the shapes and sizes desired. *a* is the punch of the dies, the lower end being concave; this punch is to be worked by means of a fly press, or by other convenient means. *b* and *c* form the two parts of the lower die. The parts *a*, *b* and *c*, are of steel; and it will be seen that the part $c^1$ of the lower part *c* of the lower die rises into the part *b* of the lower die, and the part $c^1$ is sunk to correspond with the punch *a*. It is important that in using the matters in a state of powder or dust, that the successive quantities put into the dies should be (as nearly as may be) of the same weight, and, in order to save the trouble of weighing, I have devised a measuring instrument, which being forced into the prepared powder or dust will take up at each time a regulated measure thereof, and then deposit the same into the lower die. Figures 2 and 3 show two sections of this instrument; in one case the instrument is shown as having just been filled, and in the other figure the instrument is shown as having been emptied. *d* is the handle, which is fixed into the tube *e* by means

of a set screw $d^1$, or by other convenient means, and according as the handle $d$ is less or more into the tube $e$, so will the quantity measured by the instrument be more or less. $f$ is another tube, which is closed at its lower end; this tube slides freely within the tube $e$ and $g$ is another tube which slides over the outer surface of the tube $e$; and the tubes $f$ and $g$ are fixed together by the screw $h$, which passes through a slot formed in the tube $e$, which slot allows the tube $f$, $g$ to slide up and down, the end of the handle $d$ determining the extent of such sliding. When the tube $c$ projects beyond the tubes $f$ and $g$, as is shown in Figure 2, it is pressed into the powder or dust, by which the end becomes full, taking care that in repeatedly filling the same the dust or powder from which the successive quantities are taken is not beaten down or compressed so as to cause the measure to make a materially greater quantity at one time than another. The measure of powder or dust being thus taken up, is to be deposited into the lower die, $b$, $c$, by moving the handle upwards whilst holding the outer tube, $g$, the pill is then to be finished by causing the punch or upper die $d$ to descend into the die, and thus, by one or more blows, to consolidate the powder or dust. The upper die $a$, and also the part $b$ of the lower die, is then to be raised up, when the pill may be removed. I have not thought it necessary to show dies for making different shaped medicated lozenges, as a workman acquainted with the making of similar dies for other purposes will readily make the proper punch and lower die to produce the proper size and shape of lozenges desired. It will be proper here to remark that this invention, when making pills, is particularly applicable when using matters readily soluble in the stomach, such as deliquescent salts used medicinally, the carbonates, tartrates and nitrates of soda and potash, and other matters, according to the judgment of the medical man, and the invention is also applicable when less soluble matters are used combined with others readily soluble in the stomach.

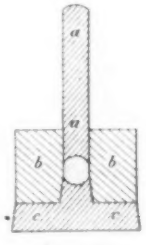

FIG. 1

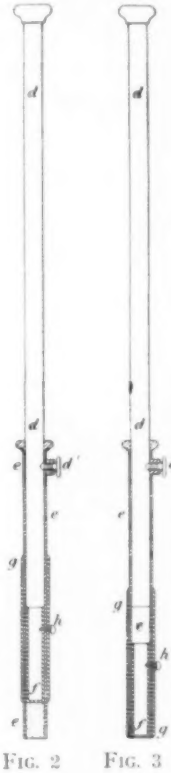

FIG. 2



FIG. 3

"* * * * And I have found that the powder or dust of black lead may be rendered solid with more certainty by means of pressure in dies by withdrawing the air from the dies, and from the powder or dust of black lead therein, before operating by pressure, and such is the case in respect to making pills and medicated lozenges, but owing to the small quantities of matter operated on when making pills and lozenges, I have not in practice found it necessary to exhaust the air in these latter cases. * * * * * *

"And I would state that I am aware that clay or brick earth has been formed into bricks, tiles, and other articles, by pressure in dies when in a state of dust or powder, and then burned in kilns, and patents have been granted for such means of making bricks, tiles, and other articles from brick earth or clay and burning; and I mention these manufactures in order to state that I do not claim the rendering powder generally into solid forms by pressure, and then subjecting the same to burning. But I do strictly confine my invention to the following improvements:

"First, I claim the mode of manufacturing pills and medicated lozenges by

causing the materials, when in a state of granulation, dust or powder, to be made into form and solidified by pressure in dies.

"Secondly, I claim the mode of preparing or treating black lead when in a state of powder, granulation, or dust, by pressure in dies, so as to solidify the same.

"In witness whereof, I, the said William Brockedon, have hereunto set my hand and seal, this eighth day of June, in the year of our Lord one thousand eight hundred and forty-four. "WILLIAM (L. S.) BROCKEDON."

At an early date it was observed that pills made with adhesive material often interfered with and prejudiced the desired action. The underlying object of this invention was to compress medicinal agents in a state of granulation, dust, or powder without the use of gummy matter or other adhesive agents commonly employed in the manufacture of pills and lozenges. The goods made by this process were known for many years as "compressed pills." The patent was put into operation and the pills brought early to the attention of the pharmaceutical profession through the press, as is shown by the following extract[5]:

"We have received a specimen of bi-carbonate of potash compressed into the form of a pill by a process invented by Mr. Brockedon, and for which he has taken out a patent. We understand the process is applicable to the compression of a variety of other substances into a solid mass, without the intervention of gum or other adhesive material. Mr. Brockedon has promised to favour us with a detailed account of this process for publication in an early number."

This note shows that Brockedon put his invention into practical use, and subsequent data corroborate the fact that his goods were continuously on the market, both in England and America, for many years.

Mr. Charles Killgore, one of the pioneers in the manufacture of tablets in the United States, relates[6] the following incident showing the early importation of "compressed pills" into the United States:

" 'Compressed tablets' were commercially imported in 1854 by E. Milhau, a druggist of New York City, at the request of Commodore M. C. Perry, who first procured them in London. The commodore was very anxious to take some of these medicines with him on his trip to Japan. Mr. Milhau did not have this form of medicament in stock and was compelled to place the order abroad, which resulted in considerable delay. The day Commodore Perry received orders to report at Hampton Roads for his final instructions he called on Mr. Milhau and requested that he forward the compressed pills to him if they arrived in time to reach him before sailing. The goods were received in sufficient time to comply with his request."

One of the earliest American druggists to keep Brockedon's goods was Frederick Brown, as shown by the following letters to the writer:

"Philadelphia, Pa., January 8, 1913.

"L. F. Kebler, Chief Drug Division, U. S. Dept. of Agriculture, Washington, D. C.:

"Dear Sir—We were duly in receipt of your favor of December 27, 1912, and have endeavored to find out something definite as to the sale of compressed Potassium Bicarbonate and Sodium Bicarbonate Tablets.

"We regret that we are unable to give you definite information on the subject, as the retail branch of this business was sold in 1888, and we no longer have any

[5] Pharm. J., 1844, 3; 554. A careful search of the files of the Pharmaceutical Journal failed to reveal a description of the promised process, and it seems likely that Mr. Brockedon never carried out his intention.

[6] Private communication to the writer.

of the old records. Our treasurer, however, Mr. H. S. Robertson, began the drug business in 1860 with Frederick Brown, Sr., and he well remembers that Brockedon's Compressed Tablets were regularly in stock at that time, being quite actively in demand.

"Regretting that we are unable to give you any further information on the subject, we remain,

"Yours very truly,
(Sgd) "F. ZERBAN BROWN, President."

F. Newberry & Sons, in a letter to the "Chemist and Druggist," given in full further on, state that Brockedon's business was purchased by them in 1871, and they continued to sell his "compressed potass. and soda." Burroughs, Wellcome & Co., in a letter to the "Chemist and Druggist"[7] write as follows:

"We notice the correspondence (*24/27 A. C. S.*) with regard to the use of the words 'Tabloids' and 'Tablets' as applied to compressed drugs. The word 'Tablets' was first applied by us to this class of drugs at the commencement of our business in 1878. This form of medication had hitherto been known in this country as 'compressed pills.'"

The following correspondence dealing with historical matters also throws light on the compressed drug industry in England about 1881[8]:

"To the Editor of 'The Chemist and Druggist':

"Sir—Have we in Great Britain any drug manufacturers with sufficient ingenuity to make little pellets or discs of such simple and useful substances as chlorate of potash, carbonate of soda, etc.? If there be such, how is it that a Yankee maker of these articles is permitted quietly, but none the less surely, to establish a monopoly of the 'compressed medicines,' as they are termed in this country?

"'Have you any of these American solid cakes of chlorate of potash?' is already becoming a stereotyped query from our customers. 'My doctor recommends them as so much superior to the lozenges.'

"We are not sure whether the articles in question are strictly a specialty of the wholesale druggist, or the lozenge-maker; but whichever it may be, it is clear that patriotic and selfish motives should combine to determine him to elbow out the intruder. * * * * * * *

"Bradford, November 5. "M. ROGERSON & SON."

"To the Editor of 'The Chemist and Druggist'[9]

"Sir—We have observed the letter of your correspondents, Messrs. M. Rogerson & Son, in your last issue, and would point out that the idea of compressing pills or tablets, by whichever name they may be called, was originated by the late Professor Brockedon, the manufacturer of compressed Cumberland leads for lead pencils. He introduced, about twenty or more years since, Brockedon's compressed potass. and soda, which have ever since been on sale both in this country and America. In 1871 we purchased Professor Brockedon's interest in these preparations, and they are still well known at home and abroad. As to 'elbowing out the intruder' it may interest your correspondents to know that we have, since the introduction of the American compressed goods, remarked with satisfaction a steady increase in the demand for the Brockedon's already referred to, and the increase applies as well to foreign as to the home markets. The monopoly must, therefore, exist more in imagination than in reality. * * * * * * *

"London, November 29." "F. NEWBERRY & SON.

[7] Chem. & Drug., 1892, *40*: 785.
[8] Chem. & Drug., 1881, *23*: 510.
[9] Chem. & Drug., 1881, *23*: 555

This correspondence shows that Yankee ingenuity and perseverance were making themselves felt in the tablet industry at that early date. The "American solid cakes of chlorate of potash" referred to in the first letter quoted were probably compressed tablets of chlorate of potash and borax, free from any excipient, which were marketed in the United States by John Wyeth & Brother, Philadelphia.[10]

The manufacture of "compressed pills" (tablets) in the United States was apparently begun by Jacob Dunton, a wholesale druggist in Philadelphia. He

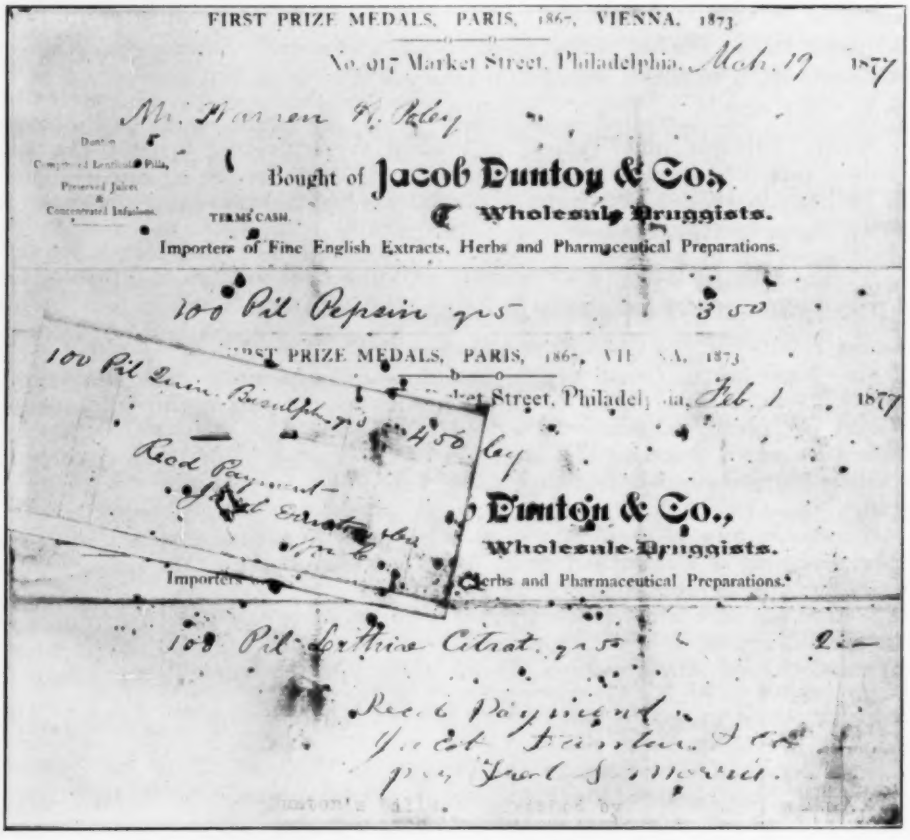
FIRST PRIZE MEDALS, PARIS, 186-, VIENNA, 1873
No. 917 Market Street, Philadelphia, Mch. 19 1877
Mr. Warren H. Paley
Bought of Jacob Dunton & Co.,
Wholesale Druggists.
TERMS CASH.
Importers of Fine English Extracts, Herbs and Pharmaceutical Preparations.
100 Pil Pepsin grs 3 50
FIRST PRIZE MEDALS, PARIS, 186-, VIENNA, 1873
Street, Philadelphia, Feb. 1 1877
Dunton & Co.,
Wholesale Druggists.
Herbs and Pharmaceutical Preparations.
100 Pil Ferri Citrat. grs 50 2—
Rec'd Payment
Jacob Dunton & Co
per Joel S Morris.

FIG. 4—Dunton's bills. (Furnished by M. Campbell, Philadelphia.)

was graduated from the Philadelphia College of Pharmacy in 1855. A letter from Dr. L. A. Edwards begins thus, "Washington, D. C., August 13th, 1862. My dear Pill-driver et Phot." It would seem that Dunton made "compressed pills" at this early date when they were actually compressed by driving. It is reported that Dunton supplied the United States Government "compressed pills" during the early sixties, but the records are inconclusive. A bill against the United States dated October 3, 1861, includes pills, but the kind of pills is left open. According to the copy of another bill, "compressed lenticular pills" formed a part of Dunton's business as early as 1867, when he was awarded a

10 New Remedies, April, 1879, p. 2, cover, vol. 8.

Paris prize, but it could not be determined whether the pills were included or not. It is interesting to note from this bill that $3.50 was charged for 100 pepsin tablets in 1877. There appears to be nothing in Dunton's private effects to throw any light on the time of his beginning pill compression. There is available, however, the complainant's record[11] of a litigation, which contains valuable data. On page 8 appears the following:

"Q. Give the date of your (Dunton's) first experiment in this matter, and your employing Mr. Murset.

"A. Some time in the winter of 1863 and 1864; by winter I mean the fall months and the early spring, say March; that was during my stay in the city; I was out of town most of the time from May until November."

On page 5:

"Q. Were you (Murset, a mathematical instrument maker) ever employed by Mr. Jacob Dunton to make a machine similar to that drawing, and if yea, state at what time.

"A. Yes, sir; it was in March, 1864; the beginning of March."

On page 10:

"Q. When did you (Dunton) first put upon the market these compressed pills?

"A. In the fall of 1869."

On page 20:

"Q. I understand from your deposition that you did not put any pills on the market between 1864 and 1869; now I wish to know how many pills you made in that period, and what use you put them to.

"A. Several thousand. I made them up for stock to sell from.

"Q. Do you mean that you made them to put upon the market, but that you did not put them on the market?

"A. I do. The greater portion of these thousand were made in 1869; the latter part of 1869.

"Q. And with what machine were they made?

"A. The second and third spoken of; the second and third machines modified after the machine of 1864."

On page 19:

"Q. Then I understand you (Dunton) now that the lever and the screw and the eccentric were in 1869 adopted and applied by you for compressing the pill or powder?

"A. They were; not on the same machine, however; on different machines.

* * * * * * * * * *

"Q. I wish to know how soon after 1864 you (Dunton) in any respect modified the machine represented in this Rough Sketch No. 2, and I wish to know at the same time of what the modifications consisted.

"A. I modified the machine described in Rough Sketch No. 2, within two or three years after 1864. The modification in this first machine, modified after the machine of 1864, was by the application of a screw to give power, and the addition of an eccentric to eject the lower plunger or lower die, to eject the pill."

On page 22:

"Q. How many varieties of compressed pills did you (Dunton) make in 1869?

"A. Over three hundred."

On page 21:

"Q. I understand you (Dunton) that you have stated that down to 1876 you had made between two million and three million pills; what machine were they made with?

[11] Jacob Dunton vs. Bennett L. Smedley, U. S. Cir. Ct., Eastern Dist. of Penn., in Equity, No. 38, April Session, 1879.

"A. Two and three machines, numbers 2 and 3 spoken of above, and similar machines."

"Q. And none of them were made on the machine patented to you in you patent No. 17490, as I understand you?

"A. No pills were made for sale on machine patented No. 174790."

This testimony clearly shows that Dunton as early as 1864 had a machine constructed for compressing tablets. It also shows that the machine was modified from time to time and that a patent for one of the machines was applied for and granted March 14, 1876.[12] The apparatus is shown in Figure 5.

The following description of the machine is quoted from the patent:

"This invention relates to an improved machine for making pills by compression; and it consists in a movable or detachable compression-chamber or powder-receptacle, in combination with two movable dies having concaved ends, the upper one of which forms the plunger, and the lower one of which is made short, and is adapted to be driven through a hole in a base piece together with the pill.

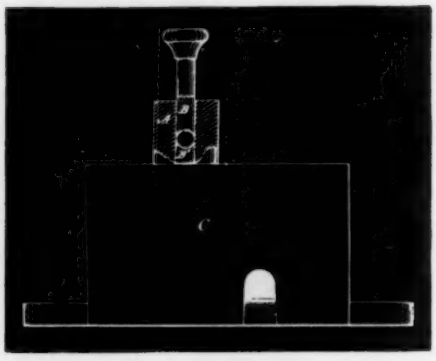

FIG. 5—Dunton's pill machine. Patented March 14, 1876. (Patent No. 174,790).

"The invention also consists in the construction of the base-piece, which is provided with a hole terminating in a laterally-discharging curved chute, by which the pill and lower die are driven out of the chamber into a convenient position; and it also further consists in the combination, with the powder-receptacle, of the base-piece, provided with guides, which permit the powder-receptacle to be shifted from its position for compressing to its position above the hole for discharging the pill without displacement, and without the delicate adjustment which would be otherwise required.

"In the drawing, A represents the powder-receptacle, which constitutes also the compression-chamber. This receptacle is perforated vertically and longitudinally with a hole, in which are accurately fitted the dies, B B′, of which B constitutes the plunger, through which the application of power is made to effect the compression. Both these dies are movable and entirely detachable, and have their adjacent ends concaved, so as to give sphericity to the pills compressed between them. The lower die, B′, is made short, and is designed to be driven out with the pill through a hole, in the base piece, C."

It will be observed that this apparatus is very similar to that of Brockedon's compressor. It will be noted furthermore that nothing appears in this patent which would indicate the use of either a lever, screw, eccentric motion or foot-power, instead of hand-power, attachment to lever.

Dunton was apparently the first to secure a process[13] patent for the preparation of materials to be used in the manufacture of tablets. This patent embodies some of the fundamental principles governing at present. He had noticed that in compressing materials containing the natural moisture of the air the cohesion of the particles was frequently insufficient to produce stability of form. He also observed that the adhesion between the material and the dies and punches was often greater than the cohesion of the particles. The invention con-

[12] U. S. Patent No. 174,790, dated March 14, 1876.
[13] U. S. Patent No. 168,240, dated Sept. 28, 1875.

sists, first, in drying the material to be compressed in order to expel the natural moisture, thus increasing the cohesion, and, second, in lubricating the die or mold. On account of its historical importance and in order that certain features may be more readily available, portions of the patent are copied herewith:

* * * * * * * * * *

"In carrying out my invention the powdered materials are first dried, preferably at a temperature of 90° Fahrenheit, so as to deprive them of the natural moisture absorbed from the air, which would have a tendency to decompose them or interfere with the compressibility or stability of compression.

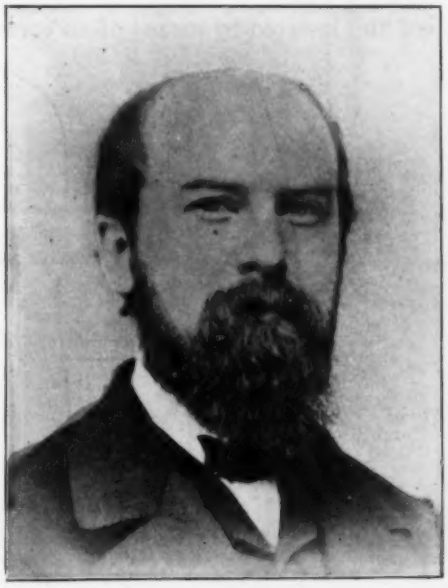

FIG. 6—Jacob Dunton.

"The materials are now in proper condition for compression and the cohesion of particles. In order to compress, however, such substances as sulphate of quinia, and other substances which leave a portion of themselves adhering to the mold after compression, which adherence prevents the formation and withdrawal of a successive pill of the same material in a perfect or merchantable condition, it becomes necessary to get rid of the adherence, and also to prepare the mold before another pill can be made. The ways which may be adopted are. first, after the pill is made, open the mold and brush out with a stiff brush as much as possible of the adhering particles, and then apply to the surface of the mold a thin film of oil, which takes or soaks up any portion of the particles which is left after brushing, and to get rid of the oil a pill of starch or other equivalent material is made, which absorbs the oil, and leaves the mold in a condition to make another pill of the original material; second, instead of lubricating the mold directly, a small portion of a liquid may be added to the powder (one percent being in some cases sufficient), which under pressure will ooze out at the surface of the pill, and act as a lubricant, so as to allow the pill to be removed from the mold without leaving any particles adhering to the mold, and leaving the latter in fit condition for the next pill."

* * * * * * * * * *

"In lubricating the mold a portion of paraffin, oil or cacao, butter of cocoa, or other equivalent material may also be used, either alone or in solution in alcohol, benzine, or other volatile liquids, the object being to apply the least quantity that will produce the desired effect, and I may also use an oily or unctuous substance combined with an absorbent material or a material which is of itself both unctuous and absorbent, for cleaning and lubricating the molds."

* * * * * * * * * *

"In manufacturing pills by compression, the herein-described method of drying the powders, before compression, at a temperature of about 90° Fahrenheit, with 24° absolute dryness (Mason's hygrometer) to prevent reaction upon the mold, and insure stability of cohesion, and lubricating the mold to prevent adhesion, and insure the removal of the pill integrally and perfect."

"Jacob Dunton.

Witnesses: "Lorenzo Westcott,

"Caspar S. Carmell."

The samples shown in Figure 7 were obtained from Professor Joseph P. Remington and Henry Blair, of Philadelphia. It will be observed that the name "compressed pills" was applied at that time, but the shape of the medication was that of the tablet as known at present. The exact date when these samples were put on the market could not be established, but the indications are that they are similar to, if not identical with, the tablets put on the market by Dunton in the seventies.

J. R. Wood[14] states that John Wyeth and Brother, in conjunction with Henry Bower, succeeded in producing a "hand press" in 1872, which materially reduced

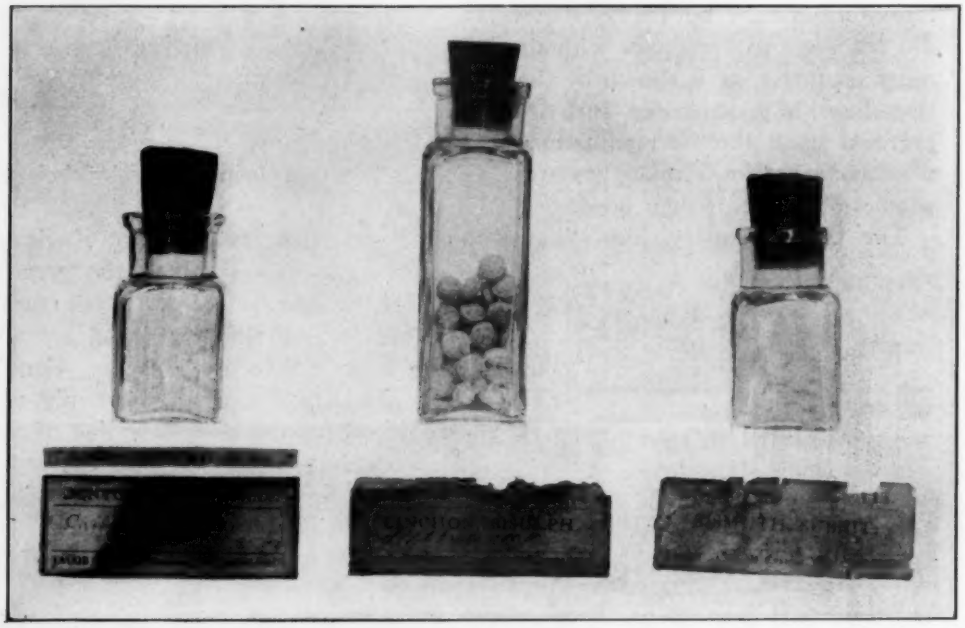

FIG. 7—Labels and bottles used by Dunton.

the cost of manufacturing tablets. This is corroborated by the following letter, except that the machine does not appear to have been a "hand press":

"Philadelphia, January 14, 1913.

"Mr. L. F. Kebler, Chief, Div. of Drugs,
"U. S. Department of Agriculture, Bureau of Chemistry,
"Washington, D. C.

"Dear Sir: Your letter of the 27th ultimo was duly received and answer was delayed on account of absence of one of our principals and beg to herewith make reply and advise that the articles you have noted published under tablet manufacture and in the Medical Record are correct.

"We have no prepared data or printed matter on hand of tablet compressing machines; from our books we glean that in about 1872 we constructed the first rotary tablet machine in our own shop by our chief mechanic; this machine was what is styled a disc machine with several dies, and improvements were constantly added and machine perfected until we had some machines that had as many as 13 dies in rotating disc and some of these machines are still in use at the present time in our laboratory.

[14] Tablet Manufacture....1906, p. 11.

"We are also the originators of the compressed hypodermic tablets and compressed tablet triturates, also compressed medicinal lozenges; these three variations were introduced by us during a period of 1877 to 1880 and other combinations of compressed tablets followed quickly according to demands made upon us by the physicians and trade. Prior to 1877 the formulae that were sold in tablet form were very few. They consisted of simple chemicals principally, such as potassium chlorate, ammonium chloride, etc., and after 1877 combinations followed. Physicians saw the convenience of this form of medication and at various times submitted different compound formulæ which were made into either tablets or compressed lozenges. After 1880, tablets having become quite popular, others entered into the manufacture of them, and various machines were invented and improved and are known as single and multiple die machines with shoe feeding devices; also different styles of rotary machines have been made since then.

"We trust this information will be helpful and regret we have no prepared data in detail that we can supply.

"Yours very truly,
(Sgd) "JOHN WYETH & BROTHER,
Incorporated. H."

The following extract from a letter written by Jacob Dunton shows that the manufacture of tablets in the United States was assuming a real trade interest:

"Philadelphia, Jany. 18th, 1876.

"I wish you would lend me a few of 'Wyeth's Compressed Quinine Pills.' I want to examine them. Some I purchased of them contained Cinchonine & I want to examine the lot they sent you.

* * * * * * * * * *

(Sgd) "JACOB DUNTON."

In conjunction with this correspondence and the great improvements in mechanical apparatus used for compressing tablets, it is interesting to record the fact that there is still in use one of the old power tablet compressing machines made about thirty-five years ago. The exact age of the machine could not be determined, but Mr. Herman Wiph of John Wyeth & Brother, in whose establishment this machine is found, writes, April 29, 1913:

"Please find enclosed one front and one side view of the oldest power tablet compressing machine in existence, as far as I know; and still in use. I have personally been using it for the past 32 years, and it was in existence several years previous to my time. It is therefore about 35 years old, and may be even 40 years old. This machine is used on any size tablet from 1/16 inch to ¾ inch in diameter, and the pressure can be regulated from the slightest to the most powerful. The material to be compressed is fed into the die, by hand, with German silver ladels or dippers of various sizes, according to the weight of the tablet. The tablet after being compressed is raised above the die level by one of the levers on the right side and is pushed off by the operator with the dipper. The other lever is used to throw the clutch for compressing, the machine making only one revolution, and is then stopped automatically by a brake, until the clutch lever is again thrown in. Only one tablet is compressed at a stroke."

This machine is similar to, if not identical with, the apparatus covered by United States patent, granted to Thomas J. Young in 1874.

Tablet making in Germany seems to have had its beginning in 1872, when Professor Rosenthal, of Erlangen, described his tablet compressor at a session

of the Physicalisch-Medicinische Socictät.[15] A translation of a part of the proceedings of the session is as follows:

"Prof. Rosenthal then exhibited an apparatus for the compression of medicinal substances in volume. This machine was originally intended for the administration of Kousso, but may be used for other medicaments also. It converts powdered drugs into small solid tablets, which may be easily swallowed. Ill-tasting drugs, in volume, or such as must possess exact dosage (Dosierung) are by this method made easy to take. The effectiveness of the medicament is in no way injured, as it disintegrates quickly in the stomach and reverts to its original state. This form of dosing has been tested with excellent results in various cases."

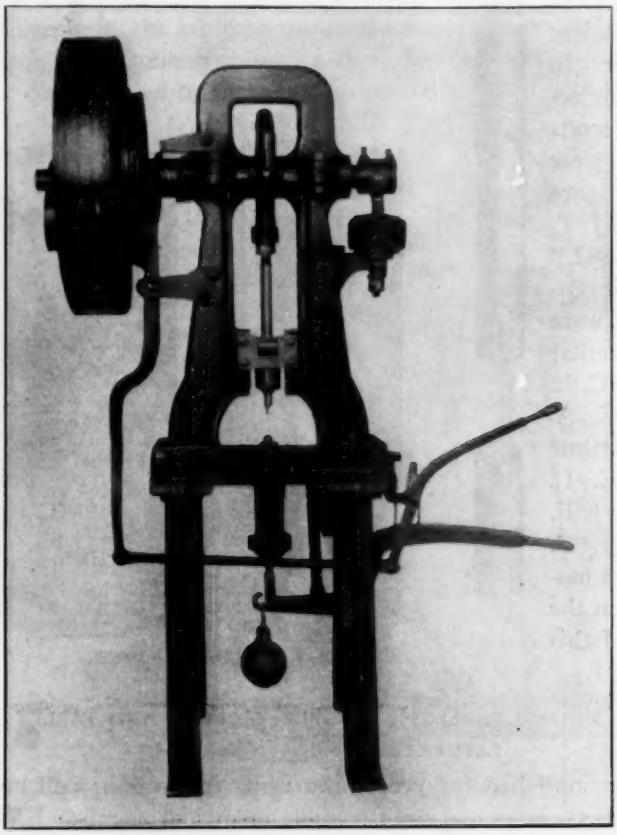

FIG. 8—Oldest known tablet machine still in operation. (Wyeth.)

A fuller description of the invention was published in 1874.[16] From this it appears that Rosenthal had no knowledge of Brockedon's invention, but believed his to be the first machine ever devised for the compression of drugs into tablet form. He says:

"Pills, powders and electuaries are still prepared and prescribed in essentially the same way as they were one hundred years ago. * * * Up to the present time all previous methods have been insufficient to solve the problem of administering large doses of medicaments offensive to taste and smell, or both."

His method consisted in compressing drugs into tablet form without the addition of foreign matter, so that they might easily be swallowed without offense to taste or smell.

The machine consists of a screw press upon a rectangular stand which may be fastened securely to a work-table or counter with clamps or screws. The iron bed-plate supporting the press has a hole drilled through its center. A slide pierced to admit a ring for a handle can be used to close or open the hole in the bed-plate, by pulling it aside. Upon the bed-plate rests the hollow cylinder *d*,

[15] Sitzungsberichte d.Phys.-Med. Soc. zu Erlangen, 1872, Heft 4 (Stzg vom 8 Juni), p. 70.
[16] Berl. Klin. Wochenschr., 1874, 11: 417.

and in this the powder is placed in the molds, *a, b* and *c* (Fig. 9.) When downward pressure is exerted by means of the screw, *e,* the loose powder is compressed into a tablet which, when removed from the cylinder, is ready for immediate use, or may be afterwards coated with gelatine. After the introduction of Rosenthal's machine, which was among the most advanced recorded at the time, the tablet became a recognized form of medication in Germany, but the home industry did not seem to keep pace with that of other countries, as is shown by the fact that English goods made such an impression upon the German public that manufacturers in Germany resorted to the scheme of using English labels to promote the sale of their goods.[17]

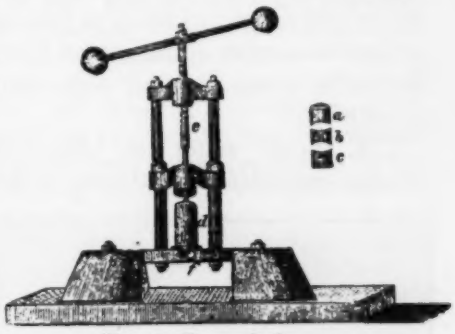

FIG. 9—Rosenthal press.

The tablet industry, like the coal-tar industry, had its origin in England. Germany, having absorbed the greater part of the coal-tar industry, was reaching out for the tablet business, but not with very satisfactory results. Conditions in Germany were apparently not propitious for the best expansion of the industry, but at any rate, the center of activity was transferred to the United States, which country has held the supremacy for the last quarter of a century.

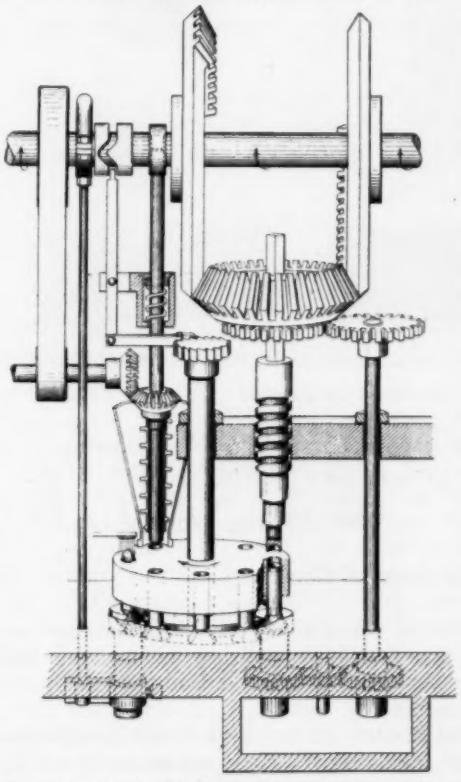

FIG. 10—J. A. McFerran's rotary machine, U. S. Pat. 152,666, 1874.

The first patent for an automatic "compressed pill" machine was issued to Dr. Joseph A. McFerran, of Philadelphia, in 1874.[18] This was what is known as the intermittent rotating machine, and the idea was probably taken from the cartridge-filling machines which had been in use for a number of years. For some reason the invention did not find proper recognition and the inventor did not receive any material profits. The same year a patent was granted to Thomas J. Young, of Philadelphia,[19] and assigned to Henry Bower, of the same place. This represents the earliest semi-automatic upright or vertical punch machine. In order to get the details of the

[17] Chem. & Drug., 1888, *32*: 712.
[18] U. S. Pat. No. 152666, dated Jun. 30, 1874, appln. filed Jun. 18, 1874.
[19] U. S. Pat. No. 156398, dated Oct. 27, 1874, appln. filed Oct. 8, 1874.

machines it is best to consult the patents themselves. The illustrations and brief descriptions are intended to give only a general idea.

Briefly, McFerran's patent consists of an intermittent rotary disc, with eight dies, an automatic feed, an upper and lower punch and a brush for removing the pills. The upper punch is raised and lowered by means of two beveled cog-wheels with a part of the teeth cut away and a spiral on the punch. The upper and lower punches are reciprocatingly rotated in order to overcome sticking.

Young's machine consists of two punches and a die. The upper punch is raised and lowered by means of an eccentric wheel, and the lower punch is raised

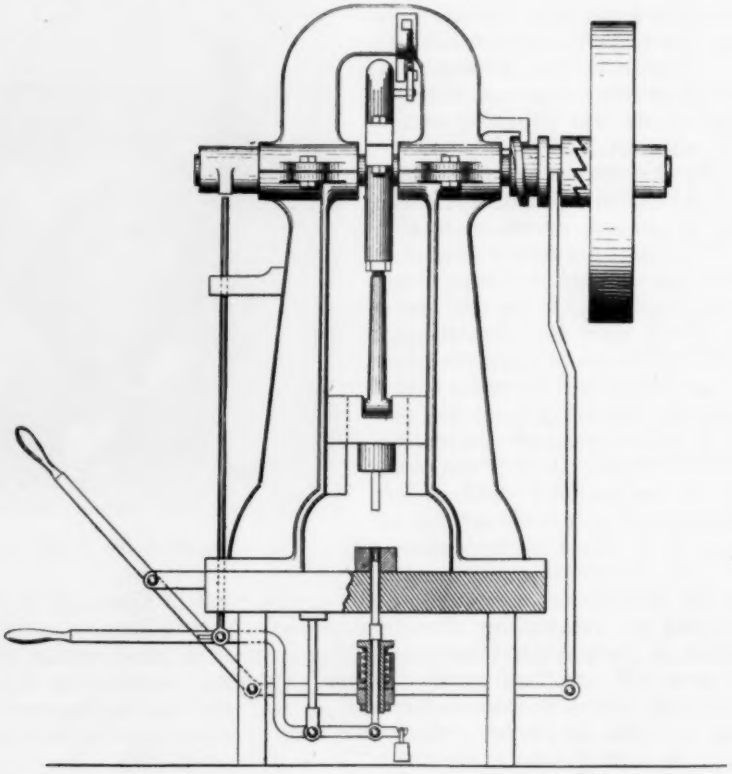

FIG. 11—I. J. Young's vertical machine. U. S. Pat. 156,398, 1874.

by a *cam* on a shaft, transmitting power through a rod and lever, and is lowered by a weight. The press is set in motion by a lever and is automatically stopped at the completion of one revolution. Feeding must be done by hand.

Joseph P. Remington, of Philadelphia, in 1875, described a simple piece of apparatus of the Brockedon type whereby the retail druggist could manufacture his own compressed medicines called for on prescription.[20] The method of operation can be readily learned by referring to the original communication.

This apparatus was improved by the inventor in 1876.[21] The vertical machine alluded to was improved in 1877 by Thomas J. Young[22] and this improve-

[20] Proc. Am. Pharm. Assoc., 1875, *23*: 620.
[21] Am. J. Pharm., 1876, *48*: 97.
[22] U. S. Pat. No. 189005, dated Mar. 27,1877, appln. filed Mar. 9, 1877.

ment was assigned to Henry Bower. In 1879 Jabez H. Gill, of Philadelphia, was granted a patent[23] for an improved "compressed pill" machine, which he assigned to Henry Bower. Two years later the same inventor was granted another patent[24] which was assigned to John Wyeth & Brother.

It should be noted that there appears to have been some affiliation between Mr. Bower and John Wyeth & Brother. In fact, the latter at some time acquired the entire tablet interests of Mr. Bower. Patents were also issued to Charles Killgore in 1882 and 1883,[25] and to J. T. and C. T. Jones in 1882.[26] From this time forward inventions in tablet machinery were numerous. The most familiar names in the industry are C. L. Jensen, F. S. Hereth, C. A. Tatum, E. C. Clark, Arthur Colton, E. V. Pechin, E. L. Richards, E. D. Dühring, J. F. Buckley, and A. M. Hance. A list of the patents for tablet machines consulted is given in the bibliography at the end of this paper.

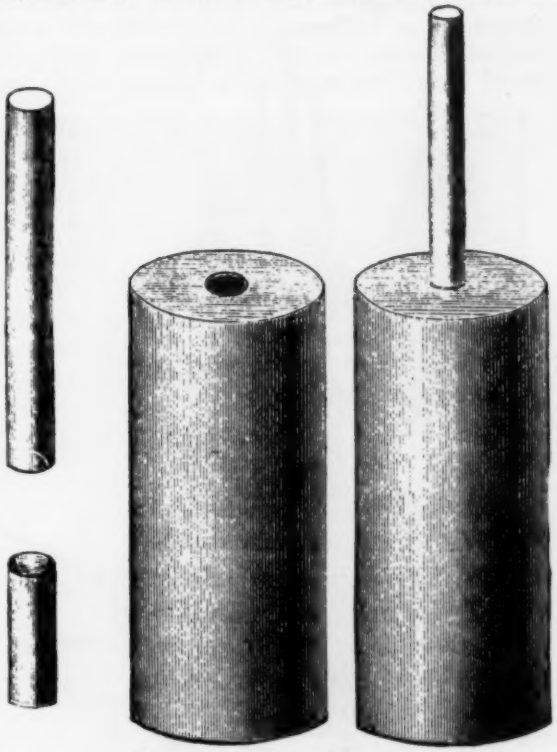

FIG. 12—Remington pill press.

TABLET TRITURATES (MOLDED TABLETS), SOLUBLE TABLETS, AND TABLET SATURATES.

The homeopathic profession[27] had for years been using triturations and medications in the form of pellets, saturated with suitable medicinal agents. Efforts had been made from time to time to bring the several professions of medicine closer together on the subject of medication. In 1877 Dr. H. G. Piffard read a paper[28] before the New York Academy of Medicine on "The Use of Certain Triturations," in which he called attention to some of the advantages of triturations. He gave the homeopathic profession credit for their development, but did not think any one should enjoy a monopoly of their use. Some of the triturations mentioned he had "compressed into convenient doses." This article appears to represent Piffard's contribution on the subject of tablet triturates, but it clearly shows that he was the first to have recorded the fact that he had

[23] U. S. Pat. 215452, dated May 20, 1879, appln. filed Mar. 28, 1879.

[24] U. S. Pat. 251678, dated Dec. 27, 1881, appln. filed Dec. 7, 1881.

[25] U. S. Pat. No. 260578, dated Jul. 4, 1882, appln. filed Nov. 16, 1881; U. S. Pat. No. 276828, dated May 1, 1883, appln. filed Aug. 22, 1882.

[26] U. S. Pat. 256573, dated Apl. 18, 1882, appln. filed Dec. 9, 1881.

[27] Hahnemann, Organon, 4th ed., 1829, p. 298 (foot-note to paragraph 283). *Id.* 1st Am. ed. from the 4th German ed., 1836, pp. 144 and 207. U. S. Homeopathic Pharmacopœia, 1st ed., 1878.

[28] Med. Rec., 1877, *12:* 756.

"compressed into convenient doses" triturations, and had brought them to the attention of the medical profession.

Dr. R. M. Fuller,[29] in speaking of Dr. Piffard's work, says:

"Dr. Piffard has found that a plate three millimetres in thickness, containing holes six millimetres in diameter, will produce tablets of about one decigramme in weight, while a plate four millimetres in thickness, with holes eight millimetres in diameter will produce tablets of about two decigrammes in weight."

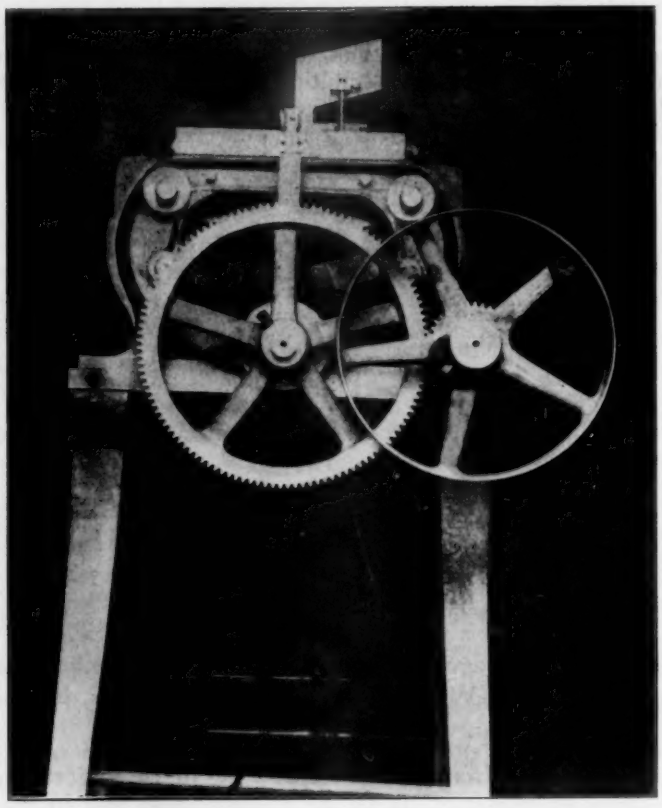

FIG. 13—Killgore machine. Patented in 1883.

Dr. Robert M. Fuller is, however, undoubtedly the originator of tablet triturates and the moving spirit in placing the industry on a substantial basis.

In 1878 his first contribution, entitled "Dose Dispensing Simplified, an Easy, Economical, and Accurate Method of Dispensing Medicines in a Compact and Palatable Form," appeared.[30] In this paper he described "soluble tablets," "tablet triturates," and "tablet saturates." "Soluble tablets," as made by him, consisted simply of certain medicines made into a soluble paste with the aid of sugar of milk and alcohol or water, and molded into form. In some instances, however, he found it necessary to employ a more effective excipient than sugar of milk. His purpose was to prepare a tablet readily soluble or disintegrable

[29] Med. Rec., 1878, *13:* 185.
[30] Med. Rec., N. Y., 1878, *13:* 184.

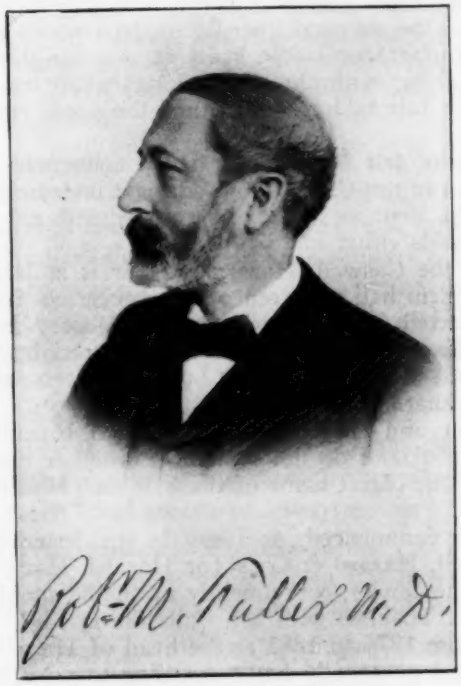


FIG. 14—Robert M. Fuller.

in the mouth or in a spoonful of water. His "tablet triturates" consisted of triturations of metallic, mineral and vegetable matter, such as were discussed by Dr. Piffard in the paper referred to. These preparations were mixed into paste with alcohol or water, according to the adhesiveness required, and the paste molded into any size desired.

Tablet saturates are made by first molding sugar of milk into convenient form and saturating the blanks by immersing in the liquid to be used for medication, or dropping it upon them by means of a pipette. The term "tablet saturates" is now seldom used in practice. Dr. Fuller in the same article describes somewhat in detail the apparatus he used for the manufacture of soluble tablets, tablets triturates, and tablets saturates.

In 1882 the same investigator presented another paper before the New York Materia Medica Society, entitled "A Convenient Method of Dosage and Administration. The Process of making Tablets of Simple and Compound Powders, including Triturations, Hypodermics, etc."[31] This contribution is an amplification of the work described four

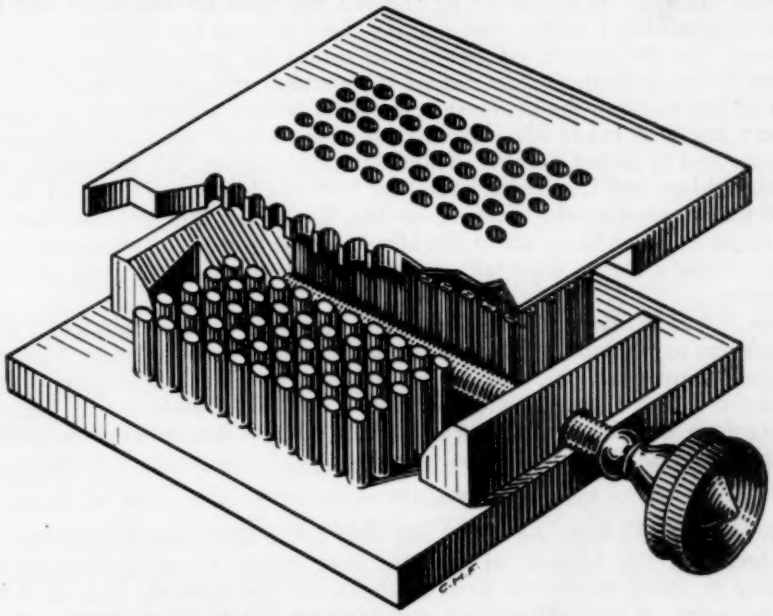

FIG. 15—Fuller's early mold.

[31] Med. Rec., N. Y., 1882, *21*: 311.

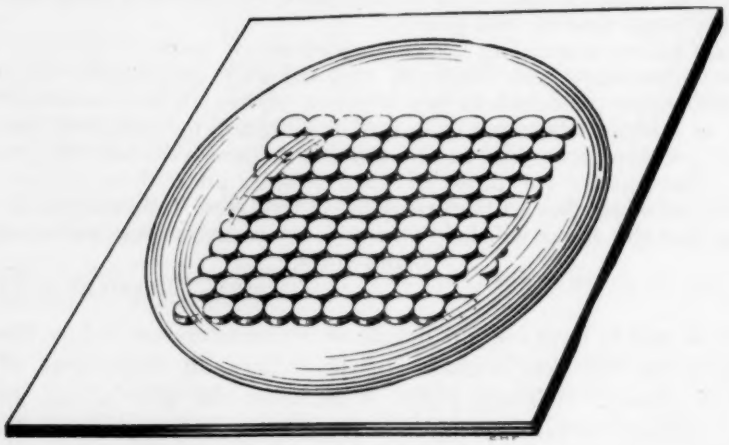

FIG. 16—Fuller's tablet saturate device.

years earlier. In it he gives another form of tablet mold, an illustration of which is given in Figure 17.

Dr. Fuller says in this article: "The idea of their adaptability for this purpose was the outgrowth of general laboratory practice in pharmacy and chemistry during 1861 to 1864. * * * * * The triturations were prepared in the manner elaborately and interestingly described in a text-book, used in connection with my earliest experiments, and entitled Mohr & Redwood's 'Practical Pharmacy,' and published in London in 1849. * * * * *" The method in question which assures the same accurate results as obtained by the process of compression, was the outcome of a long series of experiments made in this line

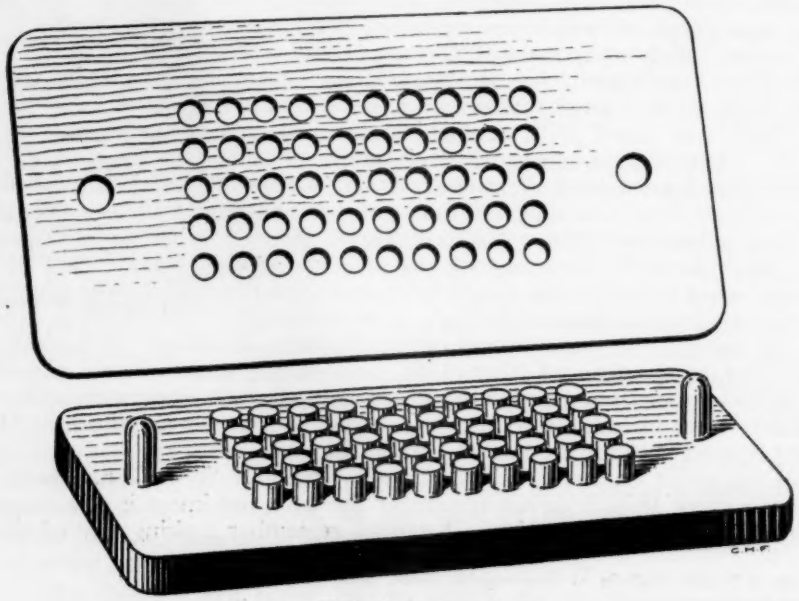

FIG. 17—Fuller's improved mold.

as early as 1861, before the system of compression was generally known or adopted in this country.

Dr. Fuller is fortunately still living and contributes the following letter, detailing briefly his early connection with the evolution of tablet triturates:

"Schenectady, N. Y., August 15, 1913.

"Dr. L. F. Kebler, Chief of Drug Division, Bureau of Chemistry,
Washington, D. C.:

"Dear Sir—Agreeable to your request of January 10th ult., and also further correspondence from Dr. Fraser and yourself, I am writing you a brief statement of my claim as the originator of the making of tablets in this country.

"Having received considerable printed matter from me and being familiar with the two papers prepared and read by me, the one under date of February 21, 1878, before the New York Academy of Medicine, and the other under date of February 23, 1882, before the Materia Medica Society, and also having at your command many articles and editorials with reference to my work along the line of the tablet industry, I feel sure that no detailed statement is necessary at this time.

"In the spring of 1861 I was employed in a drug store where I first began the practical work of making pills, subsequently called tablets. I subsequently took a full course in chemistry in the laboratory of Union College from 1861 to 1863.

"During all this time and for many years, I was greatly interested in the industry of making apparatus with which to find a convenient method of making compressed tablets and Tablet Triturates. At first, in 1861, the process for making porous pills was very simple and finally resulted in producing the 'Tablet Triturates' as now used as well as the compressed tablets.

"My work has been continued from that time—1861—with more or less interest, and while I am not inclined to be presumptuous, I might say that I was known as the 'Father of Tablet Triturates.'

"I was well acquainted with Dr. Piffard, but never knew that he made a claim as the discoverer of any tablet process. I well know that I first brought attention of the medical profession to the 'Tablet Triturates.' Dr. Piffard and I worked together long after I had invented the process. I have abundant proof among my private papers of the above facts but too much space would be required to go farther into details at present.

"Yours truly,
(Sgd) "ROBT. M. FULLER, M. D."

Numerous editorials and trade references are available to show Dr. Fuller's connection with the early evolution of this industry. The following editorial appears in "New Remedies"[32]:

"Dr. Fuller's method of subdividing remedies (see page 69) so as to enable them to be administered in an agreeable form, and in uniform and adjustable strength, with the least expenditure of labor, appears to be a step in advance of previously-known pharmaceutical methods, and, like some other inventions of practical utility, surprises us by its simplicity, and makes us wonder why it was not suggested long ago. * * * *

"So far as we are able to judge from examination of Dr. Fuller's specimens, and from seeing his processes of manipulation, there is now little reason why they may not prove to be among the most successful of the methods yet proposed for the accurate subdivision of doses.

"Certain it is that Dr. Fuller is entitled to great credit for the persistency with which he has worked out the problem, and overcome its difficulties."

[32] New Remedies, Vol. VII, 65, March, 1878.

In a circular published by Boericke & Tafel, April, 1878, appears the following:

"New Pharmaceutical Preparations, in Separate Doses, in a compact and palatable form. Soluble Tablets, Tablet Triturates, Pill and Tablet Saturates, made according to Dr. Robert M. Fuller's method as published in the Medical Record of March 9, 1878."

In a circular to the trade issued April 8, 1878, by Caswell, Hazard & Co., appears the following:

"Soluble Tablets, Tablet Triturates, Pill and Tablet Saturates, made according to Dr. Robert M. Fuller's method."

Fraser & Company, in a leaflet issued December 10, 1881, speak of "Tablet Triturates made according to method proposed by Dr. Robert M. Fuller."

The cut shown in Figure 18 was circularized to the trade in 1886.

A letter from Messrs. Boericke & Tafel, of Philadelphia, shows that the form of medication advocated by Dr. Fuller was put on the market soon after his contribution appeared in print. The letter is as follows:

FIG. 18—Package of tablet triturates.

"Philadelphia, January 7, 1913.

"Mr. L. F. Kebler, United States Dept. of Agriculture,
Washington, D. C.:

"Dear Sir—We have endeavored to find some data in reference to the early history of the manufacture of tablets and find that we can give you very little information. We published from 1871 to 1885 a quarterly bulletin announcing anything new of interest to physicians in our school. In the May, 1878, issue we find an article on the use of certain triturations by Dr. Piffard taken from the December number of the Medical Record, which is no doubt the article you refer to. We find no mention made of the announcement of the manufacture of tablets until the August, 1879, number in which there is a statement made that we can now furnish tablet triturates giving prices, etc. The following statement was taken from the May, 1884, number:

" 'We have been subjected to some criticism for pushing these goods, and will take this opportunity to briefly state our position in the matter:

" 'In the December 1, 1877, number of the Medical Record, there appeared an article that had been read before the New York Academy of Medicine by Dr. Piffard, calling attention to the homeopathic triturations, and recommending the use of our first and second decimal triturations of a number of the active drugs, it being asserted that they were found to be more prompt and reliable than these same drugs when exhibited in the ordinary mode and form.

" 'In February, 1878, Dr. Robert M. Fuller read a paper before the same body, in which he referred to Dr. Piffard's address, and proposed as a convenient mode of dispensing these triturations, an invention of his, which he styled "Tablet Triturates," which consisted in forming of these triturations suitably sized tablets, each of which constituted a dose.'

"The idea found much favor, and to supply the demand, we prepared a list

of our regulation triturations, of which any given trituration is made into tablets containing the usual dose of two grains.

"Later on,[33] tablets containing larger proportions of crude drugs were ordered by old-school physicians, and the trade assumed such proportions that we prepared the list, again published in this number, styling them 'Dosimetric Tablet Triturates,' in contradistinction to those of the regular homeopathic triturations.

"They are prepared according to Dr. Fuller's method with one difference, i. e., substituting glass plates for those of hard rubber, an obvious advantage, the increased cost of which has so far prevented others from following suit.

"Trusting that the above will help you in your investigations, we remain,

"Yours truly,

(Sgd) "BOERICKE & TAFEL."

Dr. Fuller is said to have laid the details of his investigation before Horatio N. Fraser, who at the time was in charge of the prescription department of a large New York pharmacy. It is also stated in literature that after a vain attempt to induce his employers to take up the industry, Fraser started the manufacture of molded tablets in a modest way in 1881. The records show that Caswell, Hazard & Co. were prepared to supply physicians with soluble tablets and tablet triturates, made according to the method of Dr. Fuller, as early as April 8, 1878. In a circular issued April 1, 1878, by Boericke and Tafel appears the following statement:

"Acting on Dr. Robert M. Fuller's valuable and eminently practical suggestions as set forth in his article above mentioned, we are engaged in getting ready a line of goods in conformity therewith * * *."

Dr. Fraser[34] in discussing these matters, says:

"I am glad you wrote me the letter about the circulars which seem contradictory, because it gives me a chance to say some things which I would not have bothered you with before, but which seem necessary under the circumstances.

* * * * * * * * * *

"My fire, some years ago, destroyed all my papers and I had no copy of the circular, photograph of which you sent me, but I saw it in Dr. Fuller's office when I was in Schenectady and both recognize and remember it.

"While there I also saw a list of Wyeth & Bro. dated 1877, in which no mention was made of the word tablet that I could find. I also saw a Wyeth list which I think was dated 1883, and which spoke of tablets. This was the first Wyeth list I remember of seeing which did mention tablets.

"I notice that I mentioned Wyeth's *New* Hypodermic tablets in my circular of 1881—I suppose from this that they had put a hypodermic tablet on the market about that time but whether they called it 'Tablet' or not I do not know, but would infer as much from the language of my circular, though I may have had the word in my mind when writing the circular, and gave it the term, myself.

"I came to Caswell, Hazard & Co.'s store under the Fifth Avenue Hotel in 1876, from being a classmate of one of the Hazards in college. I worked there until just before the first of May, 1881, and during most of this period had charge of their prescription department, consequently was there during the time when tablets were introduced to the profession. I rented my first store May 1, 1881, and opened it about the last of July in the same year.

"I also recognize Caswell, Hazard & Co.'s circular. While I had been there continuously from 1876, I do not remember the date, but know it was about that time when they first made tablets. I cannot remember making any of them at

[33] Boericke & Tafel's Bulletin of Homeopathic News, May, 1884.

[34] Private letter to writer.

Caswell, Hazard & Co.'s store until just after Doctor Fuller's first paper was read, but W. F. Ford, who was head of the surgical instrument department of C. H. & Co., and another specialty manufacturer in the same factory building, must have been experimenting and working with the molds long before that, because they had them in shape to make fair tablets at the time the paper was published.

"W. F. Ford has been dead some years, but I have just had a conversation with Clarence Ford, his son, who worked in the C. H. & Co. surgical instrument department from 1875 to 1880. He says that, as well as he can remember, his father commenced to experiment with molds either in 1876 or 1877.

"Another indication that the date on the Caswell, Hazard circular is at least about right, is that Mr. Caswell of that firm had gone out of the concern a few months after I came with them. He started the firm of Caswell & Massey and was at that time in a dispute whether Caswell, Hazard & Co. had any right to that name, for the reason that he did not sell out his interest but took a *pro rata* amount of the stock and fixtures for his share.

"Caswell, Hazard & Co. lost the suit and changed their name to Hazard, Hazard & Co. after the decision of the court. I do not remember whether they were allowed to use the trade mark with the oldest name of the firm on (Hazard & Caswell) or not.

"My personal connection with tablets commenced, as I say in my letter of October 6, when I was a clerk in Caswell, Hazard & Co.'s (or Hazard, Hazard & Co.'s, as it was after the decision of the court), consequently my name should not figure in their history until I went into business with Mr. Fairchild in 1881.

"But having been most of the time from 1876 to 1881 at the head of Hazard, Hazard & Co.'s prescription department, I personally had something to do with their manufacture, because they made them in a very small way, as shown in your photograph of their circular dated 1878, the last paragraph of which says 'and will make special rates when *100* or upwards are ordered.'

"As well as I can recollect, it was just after Dr. Fuller read his paper on tablets that either Mr. Hazard or Dr. Fuller asked me to go up to the doctor's office on a special errand. While there he showed me what he had done and the details of the process that I might start making them at once for Caswell & Hazard Co.'s business. In the course of our conversation he said that he wished to have nothing to do with the trade end of the matter, and that he wanted to give the result of his work to the profession for their benefit without any returns or profit to him; and had made Mr. Hazard promise to have no secret about any of the formulas and to patent no part of the idea or processes. He also made me promise the same thing, and I, at least, have kept both the letter and spirit of that promise.

"At that time either he told me, or Mr. R. N. Hazard told me, that the doctor had talked to other firms about his idea but that none of them could see anything in the doctor's ideas, especially as they were complicated with his ethical restrictions.

"The Hazards made the tablets in a small way for some time and I could never induce them to go into their manufacture in what I thought was a business way.

"One of my principal reasons for leaving the Hazard employ was the idea that there was a future ahead for tablets, and my business was based on their manufacture and the idea that a druggist's success depended on what he did for and suggested to physicians.

* * * * * * * * * *

"To sum up: I have no doubt but that Dr. Fuller should have the credit for precedence in the history of tablets; that either Caswell, Hazard & Co. or Boericke & Tafel made the first of them for the market, and all I had to do was the work of perfecting their manufacture, as was incumbent on me as the head of the prescription department of Caswell, Hazard & Co. at the time they

were introduced, and the faith I had in what they would do for the physician in the mechanical branch of medicine.

"I have done the best I know how to help you get at the history of Tablet Triturates."

As will readily be seen from the foregoing historical data, compressed tablets and tablet triturates, from which all other varieties originated, have had different lines of evolution. In point of time, however, the improvements proceeded almost simultaneously. Tablet triturates are either compressed[35] or molded. Their upper and lower surfaces are flat. In the case of compressed tablets the upper and lower surfaces may be either convex or flat. The three workers who stand out in the early history of the industry are Brockedon, Dunton and Fuller.

### DEFINITIONS.

The term "tablet" has been applied to solid medicines of certain forms for several centuries. Samuel Johnson[36] gave the following definition for the term "tablet" and an illustration of its use:

"A medicine in a square form.

"It hath been anciently in use to wear tablets of arsenick, or preservatives, against the plague; as they draw the venom to them from the spirits.—Bacon."

The same definition will be found in the edition of 1819 and in the reprint of 1827.

M. Baumé[37] as early as 1762 devoted several pages (526-541) to the subject of "tablettes." He also gave a number of formulæ for preparing "tablettes," of which the following is representative:

Des tablettes altérantes, qui se font à la cuite du sucre.

Tablettes béchiques.

| | | |
|---|---|---|
| Sucre | | lbj |
| Racines de Guimauve, Régliffe | aa | 3 iij |
| Iris de Florence | | 3 j |
| Gomme adragant | | 3 ij |
| Opium préparé par digestion | | gr. vj |

The same author in the second edition of his book on "pharmacie" gave the following formula[38]:

Tablettes antimoniales de Kunckel (lived 1630-1702).

| | |
|---|---|
| Amandes douces pelées | ℥ j |
| Canelle | ℥ ij |
| Petit Cardamome | ℥ ss |
| Antimoine crud préparé | ℥ ss |
| Sucre | ℥ vij |

Kunckel died in 1702 which clearly shows that tablets as then known were made previous to that time. The term "tablet" was applied to a mixture of melted camphor and white wax in 1847.[39] Chlorate of potash tablets were re-

[35] So far as records show, Dr. Piffard was the first to have recorded the manufacture of compressed tablet triturates.

[36] A Dictionary of the English Language, 1st ed., 1755.

[37] Elemens de Pharmacie, 1762, 1st ed.

[38] Elemens de Pharmacie, 1769, 2d ed., p. 707.

[39] Pharm. J., 1847, 7: 47.

ferred to in the same journal as early as 1862.[40] Burroughs, Wellcome & Co. wrote as follows[41]:

"We registered the word "Tablets" in this connection as a trade-mark, and therefore regard it as our rightful property, also because we introduced the word here, and because it is in our opinion non-descriptive, and therefore eligible for use as a trade-mark. We still employ it on some of our goods. A 'Tablet' has never been described or considered as a substance having a round or oval surface, but rather as having a flat or squared surface. In the compressed form of medication the surface is rounded or curved. Some firms have, we presume, inadvertently used the word 'Tablets' in connection with compressed drugs."

According to the "British Trade Marks Journal" of February 28, 1883, page 115, a trade-mark, No. 31,235, was issued to this firm, but apparently not solely on the word "tablets." The trade mark is in the form of a rectangular figure with the word "tablets" impressed upon it. This is quite a different matter from claiming the exclusive right to the use of the word "tablets." Additional information upon this subject will be found in the "Chemist and Druggist."[42]

The name "tablets" is sometimes restricted to tablet triturates,[43] but trade practice does not warrant such limitation. At present the designation "tablets" is a general term and cannot be said to mean any special kind of tablet.

Every indication tends to show that the term "compressed tablets" had its origin in the United States and that John Wyeth and Brother were the originators of the name.[44] Registered trade-marks No. 1001 and 1002 were issued to that firm on March 13, 1877, covering the term. The copy of a label found in the U. S. patent office records of one of the above numbered marks follows:

"Compressed Tablets of Chlorate of Potash for Hoarseness, Bronchial Irritations, Sore Throat, Ulcerations, Mercurial Salivation, Diphtheria, Croup, etc., etc.

"FOR SORE THROAT, HOARSENESS.

"Directions:—Adults should take one every hour or two until relieved, allowing it to dissolve slowly in the mouth. Children half of one as often.

"For offensive breath, no remedy will give more certain relief. Use one, two or three times a day.

"For diphtheria, croup and the more serious ailments, the physician should direct.

"JOHN WYETH AND BROTHER, PHILADELPHIA."

*Dispensary tablets.* A soluble form of medication of accurate composition, for the use of the pharmacist in preparing certain solutions, thus dispensing with the necessity of weighing.

*Dosimetric tablets.* A form of tablet triturates prepared to give accurate dosage used as early as 1884.

*Hypodermic tablets.* These are soluble tablets for hypodermic use for both human and veterinary purposes.

*Molded tablets.* This term covers any form of medication prepared in molds of the kind first brought forward by Dr. Fuller. The two sides are usually flat.

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40 Pharm. J., 1862, *22:* 40.
41 Chem. and Drug., 1892, *40:* 785.
42 Chem. and Drug., 1890, *37:* 531, 563, 603, 665, 695; 1892; *40:* 785, 817, 849, 881.
43 Remington, Practice of Pharmacy, 1907, 1199.
44 Chem. and Drug., 1883, *25:* 567.

It should be stated, however, that not all tablets with two flat surfaces, "block tablets," are molded.

*Opthalmic tablets* are tablets containing medicinal agents for the use of oculists, and the filling of their prescriptions by druggists.

*Proprietary tablets.* This term is applied to proprietaries in tablet form.

*Soluble tablets.* A general designation applied to all forms of tablets soluble in water.

*Tablet saturates.* A form of medication introduced by Dr. Fuller but at present little used, as is shown by the following letter:

"Philadelphia, February 13, 1913.

"Mr. L. F. Kebler, United States Dept. of Agriculture, Washington, D. C.:

"Dear Sir—In reference to the use of tablet saturates would state that these are not much used by doctors. Our dilution and tincture tablets, of course, are practically tablet saturates only that the tincture and dilution are mixed in proper proportion with sugar of milk and then molded into tablets, whereas the tablet saturates are made by taking the blank sugar of milk tablets and merely saturating them with the tincture or dilution. The former, you will see, is a much more accurate preparation, as the exact amount of liquid can be added to the sugar of milk so that each tablet will contain a specified amount.

"Very truly yours,

(Sgd) "BOERICKE & TAFEL."

*Tablet triturates.* A term originally applied by Dr. Fuller to molded tablets. At present, however, it is indiscriminately applied to all tablets, soluble or insoluble, having two flat surfaces. They may be made by either molding or compression.

*Veterinary tablets.* This is a term applied to tablets used in veterinary practice.

## MANUFACTURE.

### INGREDIENTS.

Experience had shown in the time of Brockedon that pills as then made with adhesives often operated to the detriment of the patient. They became hard and indisintegrable for practical purposes. Brockedon conceived the idea of compressing drugs without the use of adhesives, thus eliminating this undesirable feature. So far as the records show he compressed soluble chemicals only, and his best known tablet was "soda and potash." "Chlorate of potash" tablets were best known and made in the United States. How long the practice of compressing soluble chemicals without adhesives prevailed is not known, but there is reason to believe that these adhesives began to be used in the early seventies. It is definitely known that Dr. Fuller used them in preparing tablets proposed by him in 1878.

Tablet triturates appear to have been specially devised for molding insoluble drugs into tablet form, and there are reasons for believing that Dunton did this long before, because he had acquired a reputation at this time for his "quinine tablets," as they were then known. There was no trouble in making tablet triturates as usually understood, but the compression of insoluble agents without adhesives presented numerous difficulties. Without these agents it was necessary to use undue pressure, thus making an extremely hard tablet, which might,

and even did, pass through the system intact, would be void of medicinal action, and might jeopardize the safety of the patient. Difficulties also arose because the tablets adhered to the various parts of the compressor. Dunton, in his process patent, provided for several forms of lubrication. The ideas he advanced are fundamental and are still basic in the industry. It is reported that the secret of Dunton's success in producing "pure tablets" without the use of adhesives or foreign material was due to the fact that he made each alternate tablet of chalk, which must be looked upon as a process of lubrication, or cleaning out the mold preparatory to another operation.

The situation in the early eighties was, therefore, that the compressed tablet industry would be restricted to the manufacture of tablets from chemicals soluble in water, which placed the industry in a very awkward position in view of the fact that tablet triturates, and soluble tablets, as molded by Dr. Fuller, were not confronted with this obstacle. The desideratum was now to prepare tablets containing insoluble ingredients which would readily disintegrate in the system in order to obtain medicinal effects. An agent was needed which would break up the tablets when moistened or placed in water. It is reported that numerous investigations were made and discoveries claimed, but nothing appears in the records. If anything was discovered and used it was kept a trade secret until 1887, when Charles Killgore applied for a patent. Mr. Killgore relates the circumstances leading up to the discovery as follows:

"In the spring of 1887 Mr. Fraser called upon me and stated that he had received complaints that the acetanilid combinations did not disintegrate readily when placed in water and I told him that I would make experiments and see if the objection could not be overcome. The criticism of Mr. Fraser recalled to me an experience I had in trying to make bi-carbonate of soda tablets in 1881. In order to get a nice, smooth tablet I had added enough potato starch to the soda to keep the tablet from sticking to the dies and by so doing obtained a beautiful looking tablet and of course thought my troubles were over, but, on examining them the next day I found they went to powder on being touched. They had been near a sink in the back room and absorbed enough moisture to swell the fecula of the starch and you might as well have tried to pick up a soap bubble. Based on this experience I then made a series of experiments with acetanilid combinations and found that starch in proper quantities would accomplish the disintegration of the tablets when they came into contact with moisture, and further experiments demonstrated that it would work with a large percentage of tablets that were used. In May, 1887, I filed an application for a process patent covering the addition of starch to dried materials before being compressed, for the purpose of disintegrating them in the presence of moisture. The application was rejected on the ground that starch was used in so many products. Up to this time it had not been used in compressed tablets, but since then has come into general use, as I made no secret of it."[45]

Mr. Kilgore's application, No. 238,375, which was filed May 16, 1887, is in part as follows:

"It is well known that the administration of medicines in the form of compressed tablets or pills, while having many advantages, has been open to disadvantage arising from the slowness with which the same dissolve in the stomach.

"The object of my present invention is to form compressed tablets or pills which, while possessing all of the advantages of those heretofore employed, are

[45] Private communication.

not attended by the disadvantage above referred to; in that when subjected to moisture they rapidly disintegrate. This result I accomplish by mixing with the ordinary ingredients constituting a compressed tablet or pill a percentage of starch which will so change the character of the compressed tablet or pill that the same will not be open to the objections heretofore existing.

* * * * * * * * * * *

"In making my improved compressed tablet or pill the same is prepared in the usual manner down to the point where the preparation is ready to be submitted to the action of the pressing machine. At this point I mix with the other ingredients a percentage of starch; and having done so, the mixture is subjected to the same operations as were heretofore employed for completion of the tablet or pill.

"Since the application of my improvement is not limited to tablets or pills of any particular constituents but may be generally applied, the percentage of starch to be preferably employed will vary in different cases. Some kinds of tablets or pills require a larger percentage of starch for obtaining the desired object than others. It will be sufficient for me to mention as an example, that in making compressed tablets or pills from bismuth, it will be found desirable to add about five percent of the starch. The starch being a substance which has substantially no injurious influences, of course an excess of it is not harmful.

"The tablet or pill resulting from my invention possesses, as far as I know, all of the qualities of those heretofore made excepting that when taken into the stomach it immediately disintegrates.

"I claim a compressed tablet or pill containing a substantial percentage of starch, for the purpose of facilitating disintegration, as set forth.

(Sgd) "CHARLES KILLGORE."

The rejection of the application is given in the following notation of the Patent Examiner on the application:

"The claim would not be patentable aside from novelty in view of the dec., Tarr vs. Webb, 2 O. G., 568.

"Starch is the most commonly used dividing agent. It enters into pills, tooth-powders, baking powders, and toilet powders generally. See Griffith's Formulary, p. 516, Br. Pat. No. 1630 of 1857, and Tooth and Baking Powders in the various Encyclopædias. Such having been compressed, there is neither novelty nor invention in applicant's procedure. See also Br. No. 202 of 1870. The application is rejected."

The reasons for disallowing the patent were general and, it must be said, not very convincing. The phenomenon observed was new and its application was undoubtedly novel. The discovery was a great triumph for the industry. From this time forward its growth was simply phenomenal. All conceivable solid drugs are now compressed into tablet form, and some fluids are also incorporated, often, however, with unsatisfactory results.

It seems hardly necessary to consider even briefly the various medicinal agents compressed. They may be found in simple or composite form in the general trade price-lists. It is, however, desirable to state somewhat in detail the excipients or adjuncts used in compressing them.

### EXCIPIENTS.

The term excipient is applied to any substance other than the medicament used in the manufacture of, or which enters into the composition of, tablets or pills.

Excipients may, for convenience, be divided as follows: Liquids, adhesives, bases, disintegrators, absorbents, lubricants, and fillers.

LIQUIDS.

The liquids used consist essentially of water, ethyl and methyl alcohol, as well as mixtures of benzine and either of the alcohols. Their purpose is to facilitate granulation and to dissolve a small portion of the adhesive, thus increasing the adhesion or cohesion of the particles.

ADHESIVES.

These consist of cane sugar, milk sugar, acacia, tragacanth, glucose, gelatine, Irish moss, and dextrin. Cane and milk sugars are the most valuable and most commonly used. When they are properly employed no additional adhesive is necessary in many cases. Cane sugar is preferred by some on account of its greater solubility, while others prefer milk sugar because it makes a more porous and absorbent tablet. Cane sugar is used in the form of both powder and syrup. Acacia is employed in powder and mucilage form. The latter is more effective than the powder subsequently moistened. This adhesive must not be too freely used on account of its tendency to produce "insoluble tablets," or those which disintegrate with difficulty in the system. Tragacanth is seldom used except in cases where it is difficult or impossible to prepare sufficiently firm granulations by other means. Glucose, gelatine, dextrin, and flour are used only for certain mixtures. Gelatine in tablets is liable to become moldy, thus rendering the tablets unfit for use. Some, however, say that this criticism is unwarranted.

(To be continued.)

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## THE NEW AGE.

This is an age of social service. Never in all history has the world been so concerned in the welfare of "the other half"; never has there been such a strict inquiry into the life conditions of all peoples; and never has there been such concerted action to relieve suffering and social wrongs, as we see manifested so generally to-day. Surely the "millennium" is at hand. Well may we say with Riley:

> "This world is a curious compound, with its honey and its gall,
> With its tears and bitter crosses, but 'tis a good world after all.
> And a good God must have made it—leastwise that is what I say,
> When a hand is on your shoulder in a friendly sort o' way."

Everywhere the hand of social service is being laid upon the shoulder of the poor and unfortunate, the oppressed and the needy "in a friendly sort o' way." It is a great work and is enlistening the co-operation of all classes of people. The layman in his sphere, and the members of all professions are working side by side—each in his sphere—to bring about proper life conditions for all.—*Russell W. Bunting, D. D. S., in Lehn & Fink's Dentist's Diary.*

# Contributed and Selected

## NATIVE DENTISTS IN CHINA.

J. F. RUPERT, U. S. NAVY, HOSPITAL CORPS.

Now that China is awakening from her long slumber of seclusion and self-satisfaction, in line with her progress in other directions, many evidences of an intelligent interest in modern dentistry may be observed in the Celestial Empire. In the large port-cities, many Chinese of the better class will be seen to have visited up-to-date dental establishments by evidences of modern dental work which they display. This has been done usually by foreigners practicing in China, and in some instances has been performed abroad; but in other cases—a direct evidence of progress—very satisfactory dental work is performed by native practitioners who have been educated abroad or who have been instructed in China under the eye and direction of the men who have learned their profession in foreign lands.

While this modern dental work is the fruit of the late progressive movement in China, the native element of self-sufficiency still prevails for the greater part with the masses, and the native dentist, pursuing his practice along the same lines his ancestors have followed for centuries, still conducts his business perhaps on the very spot where his father practiced the same profession.

Throughout China, on street corners and in alleyways, the native dentist may be seen, exhibiting hundreds of incisors and molars, as evidence of his skill and as encouragement to others to add their bit of ivory to the stock already on hand, which collection probably comprises many inheritances from former generations.

His furniture consists of a table and chair. His instruments consist of the crudest forceps and scrapers made to order at the blacksmith shop. Of medicines he knows nothing. His real stock in trade are his wits and his general power of argumentation.

Silver fillings are made, but no gold work is attempted. He has no drills and the cavity is scraped out with home-made spoons. The technique of his work consists of filing silver coins and mixing these filings with mercury, which amalgam, after being inserted into the cavity, rapidly hardens; but trouble often arises later when as is likely the more or less exposed nerve resents such primitive treatment and the pseudo-dentist is at a loss for means of removing the filling. Nothing can then be done by him but extract the tooth.

The price charged for extraction of teeth is from 20 to 40 cents, local currency (about 8 to 16 cents gold), for each. Price is arranged to meet the financial standing of each individual; while earnest endeavor is made to convince the patient that *his* particular tooth is most difficult to extract and requires exceptional skill—all of which adds increased expense.

As in all dentistry practice, the Chinese practitioner will occasionally encounter cases which he would rather have had presented to the "man across the street," but the Mongolian practitioner thinks as much of his professional reputation as his more civilized *confreres,* and when such cases present themselves his wits are equal to the occasion. He dismisses the patient by stating that the tooth is a "blood tooth," and should it be extracted the patient will most surely bleed to death. This explanation should be sufficient for any one, white or yellow, but pain is not easily disposed of and in cases where the extraction of the tooth is insisted upon, the dentist will explain that as his assumption of the responsibility of extracting the tooth carries with it possibilities of grave results to his career and reputation, he cannot attempt the operation for less than $5.00. This is expected to cause the patient to seek relief at a less price, and this is the usual result.

I have seen these street-corner dentists extract teeth by fastening a strong thread about the tooth and extracting it by leverage.

However, as in the practice of medicine, so in the practice of dentistry, we find many very good Chinese practitioners who use modern methods. In Nanking, at one time the Imperial capital of China and a city with an old and important history, showing evidence of the present progress in China along these lines, a young Chinaman has established a very fine dental parlor. A large waiting room for foreigners, with the latest magazines of America and Europe upon the table, and separate rooms for Chinese patients have been provided.

This man, Dr. Yin Seong Hoh, was taught his profession by an American dentist in Honolulu. He has a complete equipment, a strictly up-to-date and well-selected dental library, and his methods and practices are in accordances with modern ideas on asepsis and antisepsis. Nanking has not more than eighty foreign residents, mostly missionary people, and this energetic young man is building up a good practice among the Chinese who have learned about some of the benefits of European civilization. Shanghai has a Chinese dental firm, Kingman & Kingman, who have a large and well-equipped establishment. The wealthy Chinese are patronizing this work, and eventually it is bound to spread to the common people, for it is not from lack of confidence in such work that it is not more general, for crude dentistry has been practiced for centuries in China, but the price charged looks extravagant to people whose one ambition in life is to make money. A rich native of the great yellow empire spends money with prodigality, but he prefers, like most of us, to spend it in other ways than patronizing his dental brothers.

# SPECIFICATION IN BUYING DRUGS.*

C. R. NOYES.

The interest and value of scientific work in pharmacy lies largely in its everyday application. I believe you gentlemen are more interested in hearing of the final results of experimental and research work as it applies to you and your daily business, than you are in the theoretical and purely scientific description of method, apparatus, etc. Following out this idea, I am going to give you the conclusions drawn from a very large amount of analytical data on the raw materials of the market. These conclusions naturally take the form of suggestions to you as to the specifications for the raw materials which you buy. In other words, I am going to try to suggest to you certain definite specifications which are good to use in buying your drugs, and through which you can take advantage of this scientific examination of market chemicals and drugs that has been done during the last six years.

From the wholesale druggist's standpoint there are two conflicting interests at work in the selection of the raw materials for sale. He is probably desirous of giving as good an article as possible and he is certainly influenced by the desire not to supply anything which does not comply with the stringent drug laws. On the other hand, he must meet competition. He must buy an article which he can sell at a profit, in competition with the articles put out by his competitors. He tries to talk "quality," but always fears that his customers believe he is trying simply to get a larger profit and that he is not giving them better goods for their money. The result of this is, that the average wholesaler is convinced that some druggists do not care for "quality" but simply wish the cheapest article they can buy. If, therefore, he is compelled, by either a real or fancied demand on the part of the retailers, to sell the cheapest grades of drugs, he is not willing to state frankly upon the label or in his catalogs the exact quality of these goods. If he were to do so, his cheaper grade would immediately, in the eyes of the purchaser, seem to be inferior to the competitive grade offered by some other house, which was not definitely classified by statements of its label. The result of this condition has been that the wholesale drug trade, on the whole, is endeavoring to market low-priced goods, and is glossing over, as much as possible, the inferiority of the goods. Gentlemen, the only cure for this condition lies with the retail druggist. If you will specify definitely what you want and insist upon having goods definitely labeled as to quality, you will get good drugs at reasonable prices, for you will force your jobbers to meet each other's prices on a common ground, instead of trying to beat each other's prices on an inferior ground. Therefore, I believe that this matter should be brought to your attention and I hope the facts which I shall give you hereafter, which facts are based on the analytical reports of thousands of samples, will lead you to realize the true situation and to remedy it by specifying your exact wants when ordering goods.

The principal conclusion which I have derived from this work, is that the best

*Read before the Northwestern Branch & Minn. State Pharm. Assoc., Feb. 19, 1914.

and safest course for the retail druggist is to specify "U. S. P." on every article included in that standard of authority, the Pharmacopœia.

First, let us see how that suggestion affects the buying of chemicals. A wholesale druggist's stock usually contains two grades of each common chemical. The commercial, or ordinary grade, he buys and sells in bulk, while the so-called "C. P." grade is bought and sold in original packages, under the label of the manufacturing chemist. You will not find "U. S. P." specified very generally on chemicals. Now the commercial grade is, to the average wholesale druggist, of unknown quality. He has been handling Epsom salts, cream of tartar, permanganate of potash, etc., in barrels and drums, for many years without considering anything but price in purchasing, and he probably knows little or nothing of their purity. Doubtless he is buying from some large producer, the most of whose product goes for technical purposes, and who may have heard of the United State Pharmacopœia, but probably pays it little regard. These drugs, being sold to the wholesaler under labels as above, are consequently sold by him under the same label. Occasionally, to be on the safe side, he may put the words, "for technical use only" or, "commercial" under the principal title, but usually, he sells the goods under the same label he finds the manufacturer using. While the wholesaler is almost entirely at fault in this matter, nevertheless it may be said that many articles bearing the label "for technical use only" are accepted by druggists without hesitation. At the other extreme from these commercial grades, you have the so-called chemically pure articles. Of course they are not chemically pure. No chemical, not even those of reagent quality, can be. But, at any rate, they are highly purified. Of "highest purity" is the proper designation. This is the ordinary selection which you may make in buying chemicals from the stock of a wholesale druggist. It is a case of "out of the frying pan into the fire." You either take chances on a poor quality or pay excessive prices for the best quality. I am not sure which is "the fire." Often, the guaranteed purity and the beauty of the so-called C. P. chemicals, do not warrant the price asked for them, and, in practice, their super-excellence is often not demanded and is wasteful. Frequently, too, by being adjusted to a different standard, they vary from U. S. P. chemicals in strength, so considerably, that they must be standardized, before using in a U. S. P. formula. This is shown by the variations in strength between the C. P. and the U. S. P. mineral acids. Is it possible, you ask, to get out of "the frying fan" without getting into "the fire?" I think it is. If you specify U. S. P. *always and only*, your difficulty will be solved. The Pharmacopœia is a thoroughly practical, as well as a scientific volume. Drugs meeting the requirements of the Pharmacopœia are, in almost every case, just good enough for medicinal purposes. What need is there of having them purer? You will be surprised to find that you will frequently pay no more for U. S. P. chemicals, guaranteed to you, than for the present bulk goods, the quality of which is unknown to you. On the whole, the Pharmacopœia committee has directed standards for purity that are not expensive to comply with. There is one consideration, however, that you must learn to overlook if you buy U. S. P. chemicals and consider prices. If you secure goods labeled with these initials, from a house that you know has graded them from their own examination you must disregard their appearance. A large part of the expense of pre-

paring C. P. articles, comes from the many re-crystallizations, re-distillations, etc., necessary to secure their fine appearance, which is so much admired. If you do not wish to pay the price, you must be satisfied with the frequently mediocre appearance of the U. S. P. articles.

As applied to chemicals, then, insist on those marked U. S. P. and refuse all goods labeled with such vague specifications as, "pure," "purified," "white," "medicinal," "redistilled," etc. These same remarks also apply to the drugs and oils that are found in the Pharmacopœia, although, in the case of these drugs you will less often find a pure grade in the average wholesaler's stock, and you will also find fewer retailers who desire to pay the price for the U. S. P. grade. I think, if you consulted the employes of the drug-department of any wholesale druggist you would find that, in nine cases out of ten, their instructions were to send the ordinary commercial or technical grade of oils and drugs, unless a better grade was specified. And this is the result of experience and not from choice. It is because the retailer has too often returned the better and higher priced article, when it was sent him without his specific instructions.

Now I propose to give you some definite examples of the difference between the U. S. P. grade of a number of articles and the ordinary grade:

*Castile Soap.* Very little of the castile soap you buy is made from olive oil, or wholly from olive oil. It is manufactured from a compound of olive oil and tallow, in varying proportions. The proportions you know nothing about. It may contain a large quantity of water or a small quantity of water. In other words, you may be paying "Castile Soap" prices for water and for tallow soap—unless you order "Soap, U. S. P." If you do, the chances are good that you will get a pure olive oil soap, containing not over 36 percent water, which is the normal and maximum amount.

*Lime.* If you buy lime for making lime water, you will get an article containing perhaps 50 percent magnesia and also probably quantities of iron and other impurities. These impurities are, to a certain extent, soluble in water along with the lime, and you cannot possibly have pure lime water, if you make it of such an article. Specify "Calcium Oxide, U. S. P.," and you will get a product of at least 90 percent purity.

*Precipitated Sulphur.* The commercial grade of this article is called "Lac Sulphur." The U. S. P. article is prepared with hydrochloric acid. In the manufacture of the cheaper article sulphuric acid is substituted. The result is that the precipitate contains a large proportion of calcium sulphate which is inert. Now, however, the manufacturers have taken a step further and "Lac Sulphur," as it appears on the market, is derived from the surface sulphur beds without purification. It is not precipitated but shoveled, and does not contain more than 40 percent or 50 percent of sulphur. The balance is clay. Why buy clay?

*Alcohol.* Commercial alcohol, as it is ordinarily sold, is 94 percent. It is to a certain degree impure. "U. S. P. Alcohol," costing but a few cents more, is the old cologne or deodorized spirits, and contains 95 percent alcohol. It is hardly at all more expensive if you consider the increased strength.

*Turpentine.* I doubt if many druggists, even the gentlemen who come here,

are aware that the United States Pharmacopœia requires that Rectified Oil of Turpentine should always be dispensed for internal purposes. The term "Rectified" is such a loose one that if "U. S. P." is not appended thereto, you may not know that this re-distillation has included the shaking out with soda, an expensive process which causes a loss and is likely to be omitted if possible. Thanks to your pure paint laws, the ordinary oil of turpentine is quite safe. You are notified on the package if you get anything that is not "U. S. P."

*Tannic Acid.* This article is almost never "U. S. P." and it may contain any amount of impurities. In this case, I believe the standard, in regard to the amount of resinous matter present, is too stringent and should be modified. If you insist on having a statement on the label as to how much resin is present, you can probably secure for yourself as definite a value without specifying "U. S. P.," and at the same time save a little on the cost.

*Oil of Eucalyptus.* As ordinarily sold, it is the Oil of Eucalyptus Amygdalina. This contains very little eucalyptol and is comparatively valueless. "U. S. P." is the specification that will get you your money's worth in this case.

*Oil of Gaultheria.* Frankly, I do not recommend the purchase of this oil nor that of Sweet Birch. Use methyl salicylate. I have personally experimented with the methods of analysis used by several houses of excellent reputation, who claim to put out the true oil of wintergreen, and I am convinced that they are deceiving themselves, when they believe that they are able to differentiate these products by chemical means. The feeling against the artificial oil is largely due—first, to the fact that it is artificial, and second, to the fact that, when first introduced, there were present considerable impurities of a phenolic nature due to imperfect manufacture. With the perfection of the processes of manufacture, the cause for this prejudice has been removed, and methyl salicylate should now be recognized to be equal if not superior to the natural oils.

*Glycerin.* On account of the fact that much the largest part of the glycerin-production goes to the making of nitro-glycerin, much of the product on the market is not "U. S. P." The two common impurities in glycerin are butyric acid and acrolein, the one very distasteful and the other very injurious. Be sure that you find "U. S. P." on the package, and do not depend on some favorite manufacturer's name, which you have been used to seeing since the days when glycerin was a by-product of candle manufacture.

*Talcum.* This is called French chalk. It is, of course, not chalk, and has not the slightest chemical relation to chalk. Nevertheless as sold it usually contains large amounts of calcium and magnesium carbonates, lime, etc. We have found as high as 50 percent of these impurities. Unless your talcum is going to be used for filtration purposes, you do not need the "Purified Talcum of the U. S. P.," but for any purpose it is desirable to avoid an excessive quantity of lime, chalk and magnesium carbonate. The way to avoid it is to specify "U. S. P."

*Rosin.* Are you aware that rosin or colophony is also in the Pharmacopœia? Rosin is so cheap that there is not anything cheap enough to adulterate it with, when you buy it whole. But if you buy the powder, look out. On account of its low melting point it is very difficult to prevent rosin from forming lumps again after it has been powdered. The result is that the powdered rosin on the market

usually contains from 25 percent to 50 percent of a filler, bran, flour, etc., put in, not to adulterate it, but to overcome the difficulty of manufacture. On the other hand, when you are ordering rosin, you doubtless do not want bran, and I would suggest that you see that the label on your goods tells you what you are getting.

*Aloes.* The same situation is found in the case of aloes. This frequently contains varying proportions of pea-meal, etc., when sold in powdered form. Now the Barbadoes aloes and the Socotrine are official in the Pharmacopœia. But Cape aloes is not, and therefore the average grade of Cape aloes is very poor, as it has no standard to measure up to. Why not require a statement, upon your purchases of Cape aloes, of the percentage soluble in boiling water? When you buy powdered aloes you have the possibility of getting insoluble matter, in the form of pea-meal, as well as in the form of dirt and impurities present on account of careless collection. Probably it would be interesting for you to know what the insoluble portion consisted of.

*Asafoetida and Benzoin.* With these you pay for the amount of alcohol-soluble matter present. The Pharmacopœia requires 50 percent of the asafoetida to be soluble, and that the benzoin should be almost wholly soluble. Of course, a large part of both of these articles, as they appear on the market, do not comply with these requirements and probably this does no harm provided you insist on knowing exactly what percentage of soluble gum resin you get.

*Anise Oil and Cassia Oil,* as they appear on the market, are largely the product of Chinese stills invented during the period when the Chinese were discovering gun powder and printing presses, and they have not been improved since. They are very crude articles and are exported in lead-lined, copper containers from which they absorb a considerable quantity of lead and copper. Almost all of the oil of cassia and a great deal of the oil of anise sold to the drug trade are these technical articles which contain at least one poisonous impurity. The pure oil may be procured for a not much higher price, but it will never be supplied unless its purity is insisted upon.

*Oil of Juniper and Oil of Lavender.* These are two oils which are official in the U. S. Pharmacopœia, but which are principally sold in the form of "imitations." By "imitations" is meant simply this: You take so much oil of juniper or oil of lavender and you add to it so much oil of turpentine or other cheap pine-distillate. You adjust the proportions so that the cost suits you, adding a little something for the labor of mixing. Then you sell it as "Oil of ———, Imitation," at low price, and many people prefer it to the real thing.

*Beeswax.* You can have beeswax or beeswax-compound. You usually have a beeswax-compound. This is another joke of the wholesale drug trade. Beeswax-compound contains anywhere from 2 percent to 70 percent paraffin wax, according to the sense of humor of the manufacturer. I must say that, in this case, the manufacturer is usually not the wholesale druggist, and, personally, I sympathize with the wholesale druggist who has to buy and sell what is wanted. Sometimes, this beeswax-compound is sold as country wax or cup wax. If you want to pay someone for melting up beeswax and mixing it with paraffin, I suggest that you insist on knowing how much paraffin they use, because the competi-

tion in this article will doubtless eventually produce a pure paraffin-wax colored to imitate beeswax, and sold as beeswax-compound, unless something is done to stop it.

*Linseed* is another thing which is usually given but very little thought. It depends for its value wholly upon the presence of linseed oil and yet ground flaxseed, or linseed meal of the market, is very frequently a product which has been partly reduced to the condition of ground oil cake. In other words, the oil has been partly removed from it. The name "U. S. P." prevents that.

There are a number of articles which do not properly come within the scope of this paper, because they are not in the U. S. Pharmacopœia, and yet I am persuaded to tell you what they are, because I seem to have been exposing some fakes and I might as well make a clean job of it.

Do you every buy crude carbolic acid? If you do, DON'T. Or, if you must, buy it on a percentage basis. It varies on the market from 95 percent to 10 percent of phenol. Sometimes it has no phenol in it at all. This is the case when you are supplied with the so-called domestic creosote oil, which is often nothing but gas-house residues.

*Coal-Tar Creosote* is another little joke originated by the chemical houses, but no longer fathered by them. In fact, the leading houses have refused to supply this article. Coal-tar creosote, used as a substitute for beechwood creosote, is a solution of phenol in water of any strength that the maker happens to decide upon. Any merits which this article may have, that the regular solutions of carbolic acid have not, are due to psychotherapy.

*Almond Meal Compound* may contain any percentage of starch, flour, etc., that the manufacturer prefers, or it may be made entirely from these articles and flavored with oil of bitter almonds. If you want almond meal made from almonds and not from peach kernels, which is just as good, I would suggest that you require a definite statement of what you are getting.

*Horse Medley* is coal dust. It is sold for black antimony but it never saw a piece of antimony. It is remarkable that the same marvelous medicinal property of sleeking a horse's coat should be produced by two such dissimilar articles as antimony and coal dust.

*Calamine.* According to authorities this is an impure zinc carbonate, depending perhaps for its medicinal effects upon its impurities, which offer an opportunity for the imagination to enter into the results that you get from it. A great deal of imagination, however, is required. "Calamine, a compound," is what you usually get. This article consists of powdered sand colored pink, either artificially, or by impurities. This must be a most efficient remedial preparation! Silica is, about, the most fixed chemical known. You will remember that it is only affected by roasting with alkalies, and the only acid that will affect it is hydrofluoric.

When you know this, you will naturally refuse to take such an article and will buy the so-called "Calamine, pure precipitated," which is on the market under the labels of the well-known chemical houses. This preparation is doubtless a little joke on the mineralogists. It so happens that, in the classification of minerals, the name of calamine has been applied in Europe, to an impure zinc

carbonate. By all of the American authorities, however, it is applied to a zinc silicate. So, when the American houses wish to put out a calamine that is beyond reproach, they follow the American mineralogists. Powdered zinc silicate is almost as inert as silica. I believe if you are willing to forego the mysterious properties of the impurities of the old calamine, you will do better by buying and selling zinc carbonate, U. S. P.

Probably I have been a little severe on some of these products and on those who place them on the market, but that has not been my purpose. Your wholesale druggist will give you what you ask for. The remedy for this situation rests with you, and not with the wholesaler. No blame attaches to you, for you have not been in a position to know what you were getting. But, you will find your wholesaler most willing to coöperate in giving you a good raw material, if you but say the word and keep right on saying the word. The word is "U. S. P."

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## BIBLICAL REFERENCES TO PHYSICIANS.

According to a writer in the *Chemist and Druggist,* biblical reference to the physician and his work are not particularly numerous, neither are they particularly flattering. In Genesis physicians are referred to only as "embalmers," a title too suggestive of undertaking to be agreeable; Job has a reference to "physicians of no value," by which he probably referred to the "irregulars" of his day; three of the texts are versions of the saying about them that are whole and need not the physician; two refer to the woman who had "suffered many things of many physicians," which Luke (himself a physician) softens to "had spent all her living on physicians." Luke, by the way, is the only Evangelist who quotes the proverb, "Physician heal thyself." This Evangelist figures in the only really complimentary text, "Luke, the beloved physician"; and there is even here nothing to show that it was his profession that made him beloved. It was Dean Swift, who preaching before the Royal College of Physicians, took for his text, 2 Chron., xvi, 12-13: "Yet in his disease he sought not to the Lord, but to the physicians. And Asa slept with his fathers," which decidedly suggests the connection of cause and effect.

# Papers Presented to Local Branches

## THE PRODUCTION AND CARE OF ANTITOXINS AND VACCINES.*

J. REVERDY STEWART, M. D.

I have been asked by the President of your Association to read a paper this evening on the production of antitoxins and vaccines, and I have tried to arrange my remarks in order to have them of interest to the pharmacist.

The enormous progress that has been made in the past twenty years, and indeed I might say in the past five years, has brought so many new angles in the treatment of disease, that it well behooves the pharmacist of today to keep in touch with the production of biologicals. For I believe—and perhaps my belief will be shared by many of the gentlemen present—that the coming way to cure a disease will be to prevent it.

I refer, of course, by such a paradoxical remark, to the question of immunity —both the "natural" and "acquired." By "natural" we refer to the power of our bodies to resist infection. This power has probably been handed down by our forefathers to a certain point, and strengthened to a great extent by our exposure to attenuated forms of many prevalent pathogenic organisms. In a broad sense, "acquired" immunity, here, may be taken to mean both the condition of those who have passed through a mild or severe form of some disease and have produced their own protection against future invasion of that particular organism, and that of those in whom immunity has been produced, at least passively, by the injection of anti-bodies. These anti-bodies are usually contained in what we commonly know as antitoxins.

Of all antitoxins, the best known, and most widely used, is the diphtheria antitoxin. As the procedure in all is practically the same, it will be sufficient for me to explain the producer's side of this one only.

In 1883, the diphtheria bacillus was first described by Klebs, and in 1884, was cultivated on artificial media by Loeffler. Hence it is commonly known among bacteriologists, as the Klebs-Loeffler bacillus. In 1888, Roux and Yersin discovered the presence of toxin in broth cultures. This bacillus, and its power to produce toxin, is the foundation, the all-necessary starting point, in the production of antitoxin for diphtheria. We keep this bacillus constantly growing in the laboratory-incubators.

The culture now used by, practically, all the laboratories in the work, was obtained from a case of diphtheria, by Dr. Parks, of the New York City Board of Health, and has proved the strongest toxin-producer so far procured, although it has been grown for many years on artificial media.

After we have the bacillus, the next step is to get the maximum toxin-produc-

*Read before the City of Washington Branch, April, 1914.

tion. This is done by growing it on specially prepared peptonized beef-broth. This broth must be made from fresh beef, freed from fat. To the extracted juice is added, 1½ percent peptone and ½ percent NaCl. It is then titrated, using phenolphthalein as an indicator. The acidity is reduced to 0.8. It is then flasked and sterilized in an autoclave at a temperature of 116° to 120° C., or about ten pounds steam pressure. This exposure to heat renders the beef broth sterile. It is then ready for inoculation.

This is done by transferring a small portion of membranous growth from our stock culture. The development is very rapid. In fact, the whole surface of the medium will be covered by a heavy membrane after twelve to eighteen hours' growth at 37° C. The growth is allowed to continue for from eight to ten days. The flasks are then taken from the incubator and examined microscopically. If pure, they are then titrated and should be found alkaline to phenolphtalein.

Filtering this culture through a germ proof filter, is the next step. After filtering, the toxin is then tested on guinea pigs to determine its strength.

This is done by injecting varying amounts. For instance, three pigs are selected, each weighing from 250 to 300 grams. They are injected subcutaneously, No. 1, 2, and 3, with 0.005 cc., 0.008 cc., and 0.01 cc. of toxin, respectively. The pig that survives is counted out of the test; the one that dies on the fourth or fifth day is taken to indicate the M. L. D. or minimum lethal dose of this particular toxin.

It is now ready for injection into the horse. I will say here that great care is exercised in selecting the animals for an antitoxin stable. They are kept in a quarantine stable until they have satisfactorily passed the test for glanders and tuberculosis. Temperatures are taken night and morning of all horses. When a horse is finally pronounced ready, the initial dose of toxin is given. This dose is usually about 0.1 of a cubic centimeter, and sometimes gives a very decided reaction. I have known on several occasions where a horse weighing from 1000 to 1200 pounds would be killed in from twenty-four to thirty-six hours following an injection of only 0.2 cc. of diphtheria toxin. The doses are gradually increased, as the immunity is established, until the horse will stand 1500 or even 2000 cc. of strong toxin. This amount would be sufficient to kill 3000 or more non-immunes. In many cases the horse will stand from 500 to 700 cc. of toxin without decided reaction. The blood is drawn from the jugular vein. From this point we will discuss antitoxin.

The blood is drawn into sterile jars containing sodium citrate solution, in sufficient quantity to bring the content to 2 percent. This prevents the coagulation, and allows the corpuscles to settle to the bottom of the jar. The jars of blood are kept in the ice box until the serum or plasma is ready to be decanted. The decanting is done by vacuum. The plasma is drawn into sterile containers. It is now ready for precipitation.

The method of precipitation has recently been decidedly improved upon by Dr. Benzhaf, of the New York Department of Health, and his method is now in use in our laboratory. I will here set forth the routine:

We first measure our plasma. To the total quantity is added 50 percent of a 4 percent NaCl solution. To the total quantity resulting from this mixture, is

added approximately 32 percent of a *saturated solution* of ammonium sulphate. This mixture is allowed to stand—usually over night. It is then heated in a water bath built especially for the purpose. The temperature of the mixture is brought to 60° C. and held there for ten minutes. It is then removed from the bath and filtered while hot through filter paper. This precipitation, called "first fraction," has thrown down the euglobulin, which is collected on the filter paper, and, later, after being pressed to dryness, is discarded.

The filtrate is measured, and to the resulting volume is added, approximately, 38 percent ammonium sulphate in saturated solution. This we call our "second fraction" and results in the precipitation of the pseudo globulins, (and is high in antitoxin value). This precipitate is collected on the filter papers and is placed between absorbent or blotting paper and subjected to a great pressure in a press arranged for the purpose. By this means all moisture is extracted and the precipitate is scraped from the papers in the form of a dry, powder-like substance, which is immediately put into parchment bags and dialyzed in running water from six to ten days, during which time it is redissolved and practically freed from the salts which have been used in its precipitation.

The resulting antitoxin is now of a decided green color, and is ready for the preliminary filtration. This is accomplished by drawing it through a pulp paper by means of a vacuum pump. After this filtration, 0.8 percent sodium chloride is added and the antitoxin is ready to test.

The testing is an all-important feature and must be accurately and scientifically performed. The method of testing is as follows:

First. We must determine the L+ dose of our test toxin. The L+ dose is the quantity of poison, not only sufficient to neutralize one antitoxin unit, but it must contain excess sufficient to kill a 250 gram guinea pig on the fourth or fifth day. The exact dose now having been determined, this amount is mixed with varying dilutions of the antitoxin to be tested. For instance, a serum which is supposed to contain 300 to 400 units to the cc. is diluted as follows: 1:200, 1:250, 1:300, etc. One cc. of each of these dilutions is mixed with the L+ dose of the toxin in the injection syringes and allowed to stand at room-temperature for one hour, then injected subcutaneously into selected guinea pigs. If the animal receiving L+ plus the 1:250 dilution, lives, and the one receiving L+ plus the 1:300 dilution, dies, we know that the unit strength lies between these values and further tests will establish it almost accurately.

The strength determined, the antitoxin is filtered through germ-proof filters and one-tenth of one percent chloroform is added and thoroughly mixed.

This is now stock and is stored in the ice box at a temperature of 40 degrees where it is kept until filled into syringes and distributed to the pharmacist upon order.

I have here samples of antitoxin showing the various stages of its preparation, which I have tried, at least, to describe to you.

There are several other antitoxins, such as tetanus, antimeningococcus, streptococcus, and recently one has been developed for pneumonia at the Rockefeller Institute. A bulletin on this subject will soon be published.

In serums we have also the normal horse serum, which has been used extensively in the control of haemophilia with splendid results.

Vaccine now comes up for consideration. Until recently when one spoke of vaccine it meant only one thing to us all—smallpox vaccine. Since 1796 vaccination against smallpox has been practiced. This work was first done by Jenner, and his observations were published as far back as 1798. In spite of this lapse of time, the etiological factor which causes the disease is still unknown. We do know, however, that with successful vaccination and quarantine, the dreaded scourge has been robbed of many victims.

Vaccination today, is quite a different problem from the procedure of the past, and is gradually wearing down the prejudice held by so many, who were sufferers, either directly or indirectly, as a result of the unscientific method of charging our vaccine points directly from the lesions on the calf, or using the scab from the arm of one person to vaccinate another. In this way it was possible to carry infections and have very sore arms, or even much more serious consequences. Such danger at the present time is practically *nil*. For we now use great care in the selection of our seed lymph, and by so doing have now almost a pure vaccine. This is put on calves selected by and under daily inspection of a veterinarian. These animals are housed in a modern building, put up for this purpose alone, and kept in the best state of cleanliness. The calf, after vaccination, is kept under observation practically day and night, until the "take" is complete and the vaccine is ready to be removed and prepared for commercial use.

The "pulp," as we term the ripened vaccine as it comes from the calf, is brought to the laboratory and goes immediately into glycerin. The effect of the glycerin is to kill off the bacteria which have gotten into the vaccine during the period of incubation on the calf, leaving the true vaccine virus unharmed and still highly potent.

After weeks in glycerin the "pulp" is finely ground and fresh glycerin is added. It is then tested both bacteriologically and physiologically. The lymph having proved pure and potent is then charged on ivory points, or filled into capillary tubes, ready for use. The lymph will remain potent for a long time if kept under proper conditions. By "proper conditions," I mean that these points and tubes should be kept in a cool, dark place. These instructions, which are printed on every package, do not seem to be taken seriously by some pharmacists, and, consequently, the lymph dries and loses its potency much sooner than it should, and thence results the "failures" which not infrequently occur with all vaccines, a matter which is of no small moment to the physician, and of these cases, I assure you the producer is kept *well* and sometimes *harshly informed*. Within the past few days, a physician told me that he had to go to several places before he found one where vaccine was kept in an ice box. He had experienced trouble with vaccine kept on the shelf at room-temperature, and did not wish to have it repeated. I want to lay stress upon the fact that biological products should be kept in a cool and fairly constant temperature. If this rule is followed the results will be better for us all.

As an illustration of this, I will say that between February 5 and 19 of this year we had the opportunity to have our vaccine tested on about one hundred children in an institution of this city. The work was done by the physician of

the institution, and he reported 100 percent of "takes" in primary cases, with no commonly called "bad arms."

The recent development of bacterial vaccines has brought a new field, both to the laboratory and the pharmacist, and their use is rapidly becoming a routine with many physicians in treating furunculosis, otitis media, pyorrhea, gonorrhea—in fact, wherever pus production is present, and in septic conditions generally.

This treatment consists of making the vaccine from the bacteria or combination of organisms causing the pathological condition. This is done by growing the bacteria on suitable media, that is selecting the medium on which the best and most rapid growth takes place. After satisfactory development, the bacteria are washed off in sterile normal salt solution, and thoroughly shaken in a bottle containing beads. This is done to separate or thoroughly break up colonies or clumps of bacteria. This accomplished, they are exposed to heat sufficient to kill all the germs present. 0.1 percent to 0.2 percent trikresol is then added and the suspension, or emulsion as it is sometimes called, is allowed to stand over night.

The next day cultures are made on various media, both ærobic and anærobic, using from 1 cc. to 2 cc. for each tube. These are incubated for from two to four days, and, if they remain sterile, the vaccine is then ready to standardize, that is to count the bacteria in each cc. This procedure is the same as that used in determining the number of corpuscles in the blood.

After standardizing, any dilution desired lower than the original count can be made.

Not only does the injection of this vaccine control the infection, but produces an immunity that is more or less lasting against future recurrence.

This method of treatment is constantly being tried along new lines, and splendid results are being reported almost daily.

The theory is, that by the injection of the killed bodies of the bacteria, the opsonic index is raised and the body is able to successfully resist the invading bacteria. Raising the opsonic index means stimulating the action of the polynuclear leucocytes and preparing them to envelope the bacteria and look after their destruction. It might be said that you prepare your army to fight the foe.

This has been proved most conclusively in the use of typhoid vaccine in the Army and Navy, and also by the many injections made recently by the general practitioner. You are all, of course, more or less familiar with this work. To those of us who are following closely the study, it looks as if the practice would become even more general than the vaccination against smallpox.

In conclusion, I want to say, that the modern and very material advance in medical science, is being built on a more firm foundation, and the component parts of this foundation are, Anatomy, Physiology, Bacteriology, Pathology and Pharmacology. Let us each do what we can for their advancement and the benefit of mankind.

# THE REVISION OF THE UNITED STATES PHARMACOPŒIA.*

JOSEPH P. REMINGTON, PH. M., CHAIRMAN, COMMITTEE OF REVISION.

The work of revising the United States Pharmacopœia is fast approaching completion, but, of course, it is impossible to announce a date of issue, because some pending and very important questions must be settled. It is expected, however, that printing in "galley" will begin July 1st.

Until 1906, the United States Pharmacopœia was accepted by the country as authoritative, when any one needed to use it for their benefit, but not authoritative when its tests interfered with what men called "business." This anomalous position was changed when the Food and Drugs Act made the Pharmacopœia the standard and the law of the land. The United States Pharmacopœia is only one out of thirty pharmacopœias used by other countries throughout the world.

The idea of an International Pharmacopœia, which would be authoritative, is regarded now as a dream of the future, but there is no good reason why all of the Pharmacopœias should not unite upon tests and rubrics, and, probably, the doses of medicines. The great difficulty in framing an International Pharmacopœia would be in selecting the articles of the materia medica and the preparations. The medical profession cannot be brought into harmony throughout the world with regard to the use of remedies against disease, and those found in an International Pharmacopœia would not be adequate, and it can readily be seen that such a book would be a very small one; as far as the United States is concerned many well-known and largely-used indigenous drugs would not be accepted by Germany, Russia, Japan, Austria and many other nations. A Pharmacopœia can never be an exploiter of new and untried remedies. That is not its function, and the book must contain a selection of drugs and medicines which are used in the various sections of the country, irrespective of special localities. Its title is the "Pharmacopœia of the United States of America." Internationalism is a grand idea and our fancy is tickled at the thought of one Pharmacopœia being used throughout the world, but the situation is not unlike that of universal peace, the disarmament of nations, and Church unity. It must be clear to everyone that, at this time, we are not ready for the culmination of these great movements. But there is no good reason why an earnest effort should not be made to induce the pharmacopœias of the world to accept as many subjects as possible upon which they can all agree; instead of an International Pharmacopœia, it would be much more practicable for each nation to have its own Pharmacopœia, with its own materia medica and pharmacy made to suit the people of the country, with an *international agreement on Standards*. This view seems to be substantially accepted by International Congresses, and every Pharmacopœial Commission hereafter will be expected to fall into line and at least make all of the very powerful and active remedies conform to one strength as, for instance, the fixing of the International Standard of arsenical preparations at one percent. An International Committee is at work endeavoring to frame tests for chemicals

*Read before New York Branch.

and assays, which will enable a physician to prescribe the best-known and most largely-used chemical substances of uniform purity throughout the world.

I am expected to speak more particularly of the present revision of the United States Pharmacopœia. It occupies a unique position; no Pharmacopœia of the world is revised upon the same plan. Pharmacopœias of the larger countries in the old world, are revised through a commission appointed by the Emperor, King, Queen, or ruler, but in the United States, the initiative comes directly from the people, and the medical and pharmaceutical professions, through a decennial convention, assembled at Washington, composed of delegates from all parts of the United States. Each body sends representatives who are believed to be most capable of determining the policy and general principles which should control the next revision. It has not been deemed wise to place the revision of such a work in the hands of men who belong to one political party, indeed your Chairman has never asked, and he does not know, how five men out of the fifty-one voted in the last presidential election, and if he did, it would make no difference in assignments of appointments. The reason given for the small honorariums or sums of money paid for services, has been the fear that money considerations would induce unworthy persons to make extraordinary political efforts to obtain control of the book to reward their friends or punish their enemies. The United States Government has been well represented in this revision, through its laboratories and the coöperation of the head of the Bureau of Chemistry, of the Department of Agriculture, Dr. Alsberg, and Dr. J. F. Anderson, Chief of the Hygienic Laboratory of the Marine Hospital Service. Several of the members of the Committee of Revision have official Government positions. It cannot be said that the Committee is not representative of the various branches of the healing art. The General Committee of 51, elected by the Convention of 1910, elect 15 of its members to have charge of the immediate revision. Each of these men become Chairmen of the Sub-committees and these Sub-committees are chosen for their especial fitness for the subject. Several of the members of the General Committee are on more than one Sub-committee. When the Executive Committee have reported on any branch of the work, the votes, in detail, from each member are reported, so that each member knows what is going on in each Sub-committee. The Executive Committee and the Chairman, both, have the right to appeal for a decision to the General Committee of Revision for a settlement. General questions, not falling immediately within the purview of a Sub-committee, have been referred to the General Committee directly. In this way, the concensus of opinion is obtained. This is a new plan for pharmacopœial revision, and is based upon the well known custom of deliberative bodies, and in fact, the principles underlying the Constitution of the United States.

The spirit which actuates both Committees and the Chairman is to get the best, without fear or favor. Publicity has been a prominent feature in this revision. For the first time in pharmacopœia building have the changes and standards and tests, been published in advance of the approval of the final text. This has been done to permit any one to frame a criticism or propose an improvement. This world-wide criticism or comment must have a limit fixed for the reception of comment or criticism, naturally, or the book would not appear for several years,

as it would be impossible to produce a work which could satisfy every criticism which could be made. Errors must, of course, be corrected whenever found and at once, but it is hoped, that with 50 or more experts reading proof, that every error will be detected before final printing.

The final draft on admissions and deletions must soon be forthcoming. There have been many admissions and more deletions. This subject has been thrashed over for nearly four years. The Convention disapproved of the admission of patented or proprietary preparations, mainly on the ground that everything in the Pharmacopœia should be free and open to all and that the Pharmacopœia should provide tests of identity and purity. If a manufacturer or owner will permit his synthetic or specialty to be introduced into the Pharmacopœia, he should sign an agreement giving to the Pharmacopœia such permission, otherwise he could secure whatever advertisement would come from the introduction of his specialty, and he might make any change in the appearance or the standard of strength or purity and the Pharmacopœia would have to frame standards and tests to suit the preparation sent out by the manufacturer. If the Pharmacopœia should introduce a synthetic without such an agreement, it would be possible for the manufacturer to have good grounds for a lawsuit and to demand an accounting and obtain damages for such loss as he believes he has sustained. In this connection a case was settled in Holland as follows:

"An action had been commenced by the Bayer Company, of Elberfeld, against a firm of wholesalers in Holland, for selling Aspirin Tablets which were not of their manufacture, thus infringing their trademark 'Aspirin.' The defense made to this action was that Aspirin was now included in the Dutch Pharmacopœia, and that, therefore, the word had come into public use and whatever rights Messrs. Bayer had previously, had now lapsed. The action was carried up to the High Court of Appeal in Holland, and Messrs. Bayer won their suit, the wholesalers being mulcted in damages, the Courts deciding that notwithstanding the word appears in the Dutch Pharmacopœia, Messrs. Bayer are still legally entitled to the word 'Aspirin' as their trademark."

If the Pharmacopœial Committee should decide to ignore the rights of an owner, and should introduce a synthetic without an agreement with him, no matter whether it was introduced under another name, the courts would rule in favor of the manufacturer or owner of the protected substance. Inasmuch as physicians can continue to prescribe the protected substance without let or hindrance, is it worth while, merely for the sake of seeing a synthetic in the Pharmacopœia to take such a step? The manufacturers of synthetics who have been consulted, have uniformly failed to give such permission and some have declared their intention of defending their rights through legal processes. An exception would probably have been made by an owner or manufacturer in a case of a patented or protected article, where the patent had a few months or probably a year to run, and, seeing a very moderate profit ahead, he might take advantage of the Pharmacopœia's introduction and give permission. The present Pharmacopœia, under the name of Acetphenetidin, admitted the extensively used and valuable phenacetin. These statements are made in order that you may understand the reasons which govern the Revision Committee in its decisions.

The Ninth Revision will differ from all those which have preceded it, mainly because much assistance has been rendered by manufacturing chemists and others, who have freely tendered their laboratory facilities and the services of their chemists, in trying out tests and standards and in perfecting detail. While this has greatly increased the correspondence, the time has been well spent because of the many valuable suggestions received. It has been necessary at times to arrange for hearings and conferences, and the effort has been made to invite every manufacturer or dealer having a special interest in the subject, to attend the hearings. A Committee of manufacturers was appointed, who were asked to get together, reconcile their differences and send a final draft to the Sub-committee. The Executive Committee of the U. S. P. did not accept every item in the report, but they did accept about 80 percent of the recommendations.

Conferences of the General Committee and the Executive Committee, have been held at the annual meetings of the American Pharmaceutical Association, and special conferences have been called in Philadelphia, of Sub-committees, with experts a number of times. In addition to this, the Committee has had valuable assistance from the local branches of the A. Ph. A. and State Pharmaceutical Associations. All of these communications have been tabulated, recorded and sent to the Sub-committees. In the preparation of the final text, by a system of collecting and recording by modern methods with card indexes, alphabetical lists and the valuable help of collaborators are grouped together, so that the editor may catch any suggestion which may correct an error or improve a process. Unlike many books, such as commentaries and text-books, a Pharmacopœia reflects the views of many persons, and is not in any sense the work of one man. It is constructive work and is republican, democratic and progressive. The plan is essentially American. There is a President and a Board of Trustees who have, during the work of revision, been kept in touch and have been supplied with circulars and the Executive Committee Letters. The Board of Trustees have the entire charge of financial affairs, making of contracts for the publication, and authorizing expenditures, but the work of revision is, of course, in the hands of the General and Executive Committees. The General Committee might be likened to the House of Representatives, and the Executive Committee, to the Senate. The Sub-committees have a parallel, in the Committees of the Senate and House of Representatives. The special Committees report to the bodies having the appointing or elective power.

For the first time in the history of Pharmacopœia making, the U. S. P. is using a method of publicity by printing before the issue of the book, in the pharmaceutical and medical journals, an abstract of the changes and standards, in order that these may be considered by all parties interested. These, must all be sent to the Chairman of the Committees of Revision before July 1st, the time fixed for beginning the printing. Any very important changes or errors discovered after July 1st, should be sent to the Chairman by telegraph.

It is not the intention, in the future, to wait for the usual period of ten years, to issue a supplement, and any addition or deletion which may become necessary, will be published, so that the book may be kept more fully abreast with the times. In this way, it is believed that the criticism made of the present and previous

pharmacopœias of being out of date, will be obviated, for the U. S. Pharmacopœial Convention is an incorporated and continuous body, each Convention taking over the property and effects of the previous Convention, new officers and committees being elected or appointed every decade.

The plan of revision has been worked out with the intention of providing the elements of stability and responsibility, and the experience of members gained in revision work, is a valuable asset in avoiding mistakes and errors of judgment. New men are elected to the Committee of Revision by the Convention, and a proper balance is sought to be maintained. Whatever criticism of this revision may be made in the future, it can never be said that every effort has not been made to have the work representative of all sections of the country.

The pharmacopœia is essentially a book of standards. Many men of many minds have contributed to its pages. It differs from ordinary books. It does not appeal to the sympathies or passions of men. It is a book without a plot. It advocates no propaganda, for *it*, itself is the propaganda. There is no exploiting of fads, no graft, no disposition to resent constructive criticism, and, now that the work is nearly finished, the Chairman declares that the sole object has been to provide pure, unadulterated, effective medicines of uniform quality, for the alleviation of pain and treatment of diseased conditions in the human race.

The lecture was illustrated with lantern slides as follows:

1. Text of the U. S. P. VIII.
2. Sub-committee No. 6 Bulletin, showing the first step in the revision—compiled criticisms and foreign standards.
3. Sub-committee No. 6 Bulletin, showing the first draft of modified text. Underlined portion differs from the U. S. P. VIII.
4. Sub-committee No. 6 Bulletin, showing the second re-drafted text as proposed for submission to the Executive Committee.
5. The Sub-committee report, as submitted to the Executive Committee.
6. Text submitted to the General Committee, for criticism and suggestions.
7. Publicity. Published Abstract of proposed changes in the text.
8. A page of the Report on Miscellaneous Galenicals, as submitted to the General Committee.
9. Circular-page, illustrating proposed text for type processes for fluidextracts.
10. Circular-page, showing a report on Inorganic Chemicals.
11. Circular-page, showing a report on Botany and Pharmacognosy.
12. Circular-page, showing a report on Assays.
13. Page, showing abbreviation and synonym to be inserted.
14. Page, showing proposed line-numbers for the U. S. P. IX.
15. Page, showing proposed paragraph numbers.
16. Page, showing proposed change in type for formulas.
17. Proposed title page, for the U. S. P. IX.

# THE PHYLACOGENS.*

F. C. WALDECKER, M. D., NEW YORK CITY.

As time goes on we appreciate more and more the wisdom and farsightedness of the immortal Pasteur, who prophesied that the day would come when it would be possible to eradicate the infectious diseases by vaccination.

Bacteriology, from the time of Leeuwenhock in the latter part of the seventeenth century to the present day, is as interesting in its evolution as any subject which medicine provides. Its development extends over a period of two hundred years and, during this time, the foundation was laid for the rapid and important progress which has been made in the last three decades.

Bacteriology has revealed that certain micro-organisms produce certain diseases and to-day we are using, in the preparation of a variety of agents, these same bacteria for their own destruction. The value of these products, in the treatment and prevention of disease, is too well known to require emphasis.

Some may think that biologic therapy has grown like the proverbial mushroom, and that the workers in this field have been over-enthusiastic in bringing into use the many products of bacterial origin. But reflect, we have been using Antidiphtheric Serum for twenty years; bacterial vaccines have been in use almost fifteen years and Koch presented his first tuberculin to the profession twenty years ago.

Therefore, while at first thought, it may seem that discoveries and methods of treatment have been presented with unusual rapidity, the therapy has in fact grown but slowly.

At the beginning of the present decade much interest was manifested by the medical profession, in and about San Francisco, concerning the reports of the extraordinary results following the use of a new class of bacterial derivatives in the treatment of acute and chronic infections. The products used were originated by Dr. A. F. Shafer of California, who presented his discovery to the profession through the San Joaquin Medical Society at Fresno, California, in October, 1910, and later through the San Francisco Medical Society in January, 1911.

These products, derived from bacteria, were denominated Phylacogens, from the Greek words, φυλαξ and γενναν, meaning "to produce a guard."

The principle upon which Phylacogen Therapy is founded, is that of mixed or multiple infection. Three theories are advanced by Shafer. First, that the human subject is at all times the host of a great variety of micro-organisms, and harbors pathogenic bacteria without harm to itself, during periods of physiologic resistance at or above par. When physiologic resistance is subnormal, and especially when solution of tissue-continuity occurs, the bacteria harbored assume pathogenic activity. Second, that practically all infections are mixed; that only in rare instances, is there infection by a single species of micro-organism;

*Read at the meeting of the Philadelphia Branch, American Pharmaceutical Asociation, April 7, 1914.

that while one species may, and usually does, predominate, the pathologic process engendered by it is accelerated and intensified by organisms of other species which are present. In other words, that in the course of an infectious disease, manifestations are due, not only to the effects of a single species of organisms, the specific infection, but also in part to the influence of other organisms, whose pathogenic role is not insignificant, and which must be combated in any successful scheme of therapeutics. Third, the growth of micro-organisms, infecting the human subject, can be arrested, and their effects neutralized, by the administration of metabolic substances generated during the development of germs in artificial culture media.

Shafer does not contend that these premises are original with himself, but that he has recognized their pathologic and therapeutic significance, and that his system of therapy by means of Phylacogen is new and a great step forward.

Instances of mixed infections will occur to all of you, as for example, gonorrhea shortly after onset, tuberculosis, and coryza. In tuberculosis, for instance, secondary infection is generally admitted to be the cause of fever, loss of weight, purulent expectoration, destruction of tissue and such other manifestations as appear in advanced tuberculosis. Further evidence of the existence of mixed infections, is the extensive use of so-called combined bacterial vaccines. Physicians many times have had cases of infection that they could improve but could not cure, through the use of a vaccine prepared from a single organism, while cure was rapidly established through the employment of a vaccine containing the predominant organism and such other bacteria as were associated therewith.

The Phylacogens are neither bacterial vaccines nor serums. They are sterile aqueous solutions of substances generated by bacteria grown in artificial media. They are prepared by cultivating a number of the common pathogenic organisms, such as the several staphylococci, streptococcus pyogenes, streptococcus rheumaticus, diplococcus and pneumoniæ, bacillus coli communis, etc. The cultures are incubated at 37° C. for a specified time, the organisms are then killed, a preservative consisting of .5% phenol added and the fluid is then filtered through porcelain. This filtrate is basic Phylacogen and commonly known as Mixed Infection Phylacogen. It is used in the preparation of the specific Phylacogens.

The specific Phylacogens for the treatment of rheumatic and gonococcal infections, erysipelas and pneumonia, are prepared by adding an equal quantity of the basic filtrate, (Mixed Infection Phylacogen), to a filtrate obtained from the predominating organism. In other words, in the preparation of Rheumatism Phylacogen, 5 cc. of a filtrate made from the streptococcus rheumaticus, is added to 5 cc. of basic Phylacogen.

Culture tests are made of each lot of Phylacogen prepared, to determine whether the completed product is sterile. Co-incidentally, safety tests of the same preparations are made by injecting relatively large doses subcutaneously, into a series of animals. Should these investigations result satisfactorily, the product is passed as safe.

As to the physiological action of these preparations, little is known, and, for that reason, Phylacogen Therapy may be objected to under the charge of empiricism. While knowledge of the action of Phylacogen is highly desirable,

the absence thereof is not a valid criticism. Pasteur knew nothing of the action of his virus for the prevention of hydrophobia; Jenner knew nothing of the action of vaccine for the prevention of smallpox; the Jesuit Fathers knew nothing of the action of cinchona bark in the treatment of malaria. These men were empirics, but who at this date minimizes the value accruing to the human family from the use of smallpox vaccine and quinine?

Investigators are busy in attempting to reveal the mysteries in the physiological action of Phylacogen. Progress in research of this kind is slow, but progress has been made, and in all probability considerable light will soon be shed upon this most interesting subject.

Clinically, Mixed Infection Phylacogen is indicated in infections classed as surgical. In this connection, it must be understood, of course, that the Phylacogens are not what might be called "pus absorbers." When pus is present, it must be liberated. Mixed Infection Phylacogen is being used with success, in the treatment of infections in a variety of locations following surgical procedure and other injuries, in puerperal infections, empyema, osteomyelitis, otitis media, carbuncle, etc., etc. It is also being employed in the treatment of hay fever and bronchial asthma. A short time ago one would hesitate to suggest the use of a bacterial product in the treatment of hay fever or asthma, as their causative factors have for years been considered other than bacterial. Suffice it to say, however, that a number of patients have received benefit from the use of appropriate vaccines or of Mixed Infection Phylacogen, and a number have been cured. So-called "asthma," due to cardiac or renal disease, or produced reflexly through pathology in the nose or throat, are not appropriate cases for Phylacogen treatment.

Gonorrhea Phylacogen is indicated in the treatment of acute and chronic complications of gonorrhea. Reports of its efficacy in acute urethritis have appeared but their number is too few to establish its value in this condition. The common complications amenable to Gonorrhea Phylacogen, are acute and chronic prostatitis, vesiculitis and the arthritis, commonly known as gonorrheal rheumatism.

Erysipelas and Pneumonia Phylacogen, as their names imply, are used respectively in the treatment of erysipelas and pneumonia, the latter only when due to the pneumococcus.

Rheumatism Phylacogen is the one of the series that has been used most largely. It is indicated in the treatment of acute and of chronic arthritis due to the streptococcus rheumaticus, and such sequelæ as chorea and neuritis.

The Phylacogens are administered either subcutaneously or intravenously. The subcutaneous method is the one of choice. It accomplishes every purpose in the majority of cases, although the results are not as rapid as from intravenous administration. As a routine measure, the subcutaneous treatment has every advantage and the intravenous method should be employed in those few cases which do not yield to the less heroic procedure.

The injection of Phylacogen is usually followed by reaction, local, systemic, or both. These reactions may be slight or marked, depending principally upon the general condition of the patient and the size of the dose. From intravenous administration, there is no local manifestation other than the slight trauma inci-

dent to injections of this kind. Following the subcutaneous injection more or less local pain, redness and swelling may result. This depends largely, however, upon the site chosen for injection. As a rule injections made slowly into locations of loose tissue are rarely followed by marked reaction, while the reaction is usually greatest when large amounts are given rapidly into the leg or arm.

The systemic response appears usually within six hours. This is manifested by chill, lasting from a few to thirty or more minutes, and an increase in the temperature. Depending again upon the general condition of the patient and the size of dose, the systemic reaction may be mild or pronounced, and following an excessive dose, there may be added to the chill and increase in temperature, nausea, vomiting, diarrhea, great depression and general numbness, etc. Such symptoms, of course, are undesirable, and when they occur, it means that the dose has been in excess.

Clinicians, at this writing, are not agreed as to the necessity of pronounced reactions, but many are of opinion that, with marked systemic response, the cure is more rapidly established. Others hold that mild reaction only is necessary.

The degree of reaction in any patient, it must be remembered, lies entirely in the size of the dose. By well controlled dosage, pronounced reaction can almost always be avoided.

The dose of Phylacogen, as with all drugs, varies with the individual patients, but, as a rule, the initial dose subcutaneously is from 1 to 2 cc. Intravenously, the initial dose is from $\frac{1}{8}$ to $\frac{1}{4}$ cc. Subsequent doses, at intervals of from twelve to forty-eight hours, are to be gradually increased, when given subcutaneously, by from 1 to 2 cc.; when given intravenously by from $\frac{1}{8}$ to $\frac{1}{2}$ cc. The usual maximum subcutaneous dose is 10 cc., the maximum dose intravenously 5 cc.

Before closing this paper, which of necessity is but a brief outline of this new therapy, I wish to take the opportunity to say a few words concerning diagnosis. It has been said that once the diagnosis is established, the treatment is easy and I think we can all agree to the correctness of this assertion in its broad sense. Diagnosis is difficult and the success of any treatment will depend upon the accuracy with which it is established. The development of exact methods of diagnosis, has advanced rapidly during the past few years and the information furnished by various laboratory tests will many times establish the diagnosis and nearly always assist in its determination. In such a protean disease as "rheumatism," for instance, accurate diagnosis is often not easy, and possibly in no other condition are so many errors in diagnosis made. This is due, in great part, to the lack of a satisfactory etiological and pathological classification of the arthritides and in part to the close clinical resemblance between them.

It has been remarked that we, as physicians, are prone to call almost any pain about the joints "Rheumatism," because then we know what we mean, although we do not know what we are talking about. One eminent medical man says, "Rheumatism has sometimes turned out in my experience to mean aortic aneurysm, cancer of the pleura, tabes dorsalis, osteomyelitis, spondylitis deformans, bone tuberculosis, syphilitic-periostitis, lead poisoning, morphine habit, alcoholic neuritis, trichiniasis, and gonorrheal infection.

Acute rheumatic fever and many of the chronic rheumatic conditions are,

beyond doubt, caused by bacteria, but to maintain that all cases of chronic rheumatism are due to germ activity, demands more evidence than we can at this time provide. Naturally, a product of bacterial origin can render no service in a condition in which the causative factor is not bacterial.

The diagnosis being correct and the case suitable, Phylacogen Therapy will, in the great majority of instances, yield prompt and pleasing results, some actually astonishing. These filtrates will produce satisfactory effects more speedily than bacterial vaccines and they are successful in many conditions in which the older agents fail. However, the Phylacogens will not accomplish the impossible—they are not "cure-alls." They have been employed for four years, during which time several thousand cases have been reported, and these indicate a high percentage of successes. Most failures, when they occur, may be considered due to lack of care in diagnosis, to indiscriminate dosage or to faulty technique.

Phylacogen, Vaccine and Serum Therapies, with the possible exception of surgery, are as exact in their scientific application as any therapy which medicine provides. Fulfill the requirements demanded, by a careful selection of cases and intelligent use and they will serve their purpose well.

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## BUSINESS EXPENSES IN GERMANY.

Apotheker Eugen Roth, of the Ludwig-Wilhelm Apotheke in Carlsruhe, has published for some years in the "Pharmazeutische Zeitung" a table showing the percentage of expense in relation to turnover. Especially interesting in the fact that during the past fourteen years the turnover resulting from dispensing has declined and that from counter-sales increased. The following table shows the percentage participation of the various items of expenditure in 1913, compared with the total turnover:

| | Percent | | Percent |
|---|---|---|---|
| Drugs and chemicals | 13.8 | Glass utensils | 2.01 |
| Specialties | 26.67 | Insurance | 1.36 |
| Dressings | 1.60 | Freights and postage | 0.85 |
| Indiarubber goods | 0.43 | Salaries and wages | 15.43 |
| Mineral waters | 1.55 | Heating and light | 0.74 |
| Stationery (labels, boxes, etc.) | 1.21 | Various | 0.86 |

The expenditure, not including taxes, rent, and interest, amount to 65.12 percent of the turnover.—*The Chemist and Druggist* (London).

# Reports of A. Ph. A. Committees

## REPORT OF COMMITTEE ON UNOFFICIAL STANDARDS.

The following portion of the report of the Committee on Unofficial Standards relates to certain crude drugs and chemicals suggested for inclusion in the next revision of the National Formulary, and by order of the Council is published in the JOURNAL in order to afford opportunity for discussion before the standards proposed are finally adopted.

Manufacturers, importers, analysts, and others interested in any of the proposed standards, are requested to send their criticisms and comments to the chairman of the committee, Geo. M. Beringer, Ph. M., 501 Federal St., Camden, New Jersey.

## APPROVED MONOGRAPHS SUBMITTED AS STANDARDS FOR UNOFFICAL DRUGS AND CHEMICAL PRODUCTS.

### AGARICUS.

White Agaric. Larch Agaric.

1. The dried fruit body of the fungus *Polyporus officinalis* Fries (Fam. *Polyporaceae*) collected from Larix Pinus Linné and Larix Siberica Ledeb.

2. Light, fibrous, somewhat spongy pieces of irregular shape, grayish-white to pale-brown externally; yellowish and resinous internally; fracture tough, fibrous; while friable it is difficult to powder.

3. The powder examined under the microscope shows numerous non-septate, narrow, mycelial threads and many cubical crystals of Calcium Oxalate .001 mm. to .002 mm. in diameter.

4. To boiling Alcohol it should yield not less than fifty percent of a resinous extract. Upon incineration it should yield not more than 2 percent of a white ash, rich in phosphates.

### ALBUMEN OVI RECENS.

Fresh Egg Abumen.

The freshly separated liquid white of recently laid eggs of the hen *Gallus domesticus* Temminck (Fam. *Phasianidae*).

### ASCLEPIAS.

Asclepias. Pleurisy Root.

1. The dried root of *Asclepias tuberosa* Linné (Fam. *Asclepiadaceae*).

2. Usually cut or broken pieces, of variable size of an irregularly fusiform root from 10 to 20 cm. long and 2 to 5 cm. thick, and occasionally branched, externally pale orange-brown, annulate above, the surface roughened by numerous fine intersecting grooves; bark thin; fracture tough, the broken surface granular and white, with inconspicuous pale-yellow wood bundles and large white medullary rays; odor slight; taste bitterish and disagreeable, somewhat acrid.

### BAPTISIA.

Baptisia. Wild Indigo Root.

1. The dried root of *Baptisia tinctoria* (Linné) R. Brown (Fam. *Leguminosae*).

2. Fleshy, 1.25 to 4 cm. thick usually cut into elongated cylindrical pieces; the crown 5 to 8 cm. thick, more or less warty and marked by stem scars; outer surface dark-brown, transversely warty, or the thicker pieces covered with a soft and friable corky layer, bearing few branching rootlets; fracture tough, the fractured surface whitish; bark-section radially striate, wood section inconspicuously radiate, porous; nearly odorless; the bark tastes bitter and acrid, the wood nearly tasteless.

### DELPHINIUM.

Larkspur Seed.

1. The dried seeds of *Delphinium Consolida* Linné and *Delphinium Ajacis* Linné (Fam. *Ranunculaceae*).

2. Irregularly tetrahedral, or by pressure

somewhat triangulate, acute at one end, obtuse or rounded at the other, about 2 mm. long and equally broad or slightly narrower; surface black or blackish-brown, deeply and narrowly furrowed, the furrows intersecting so as to give a sharply tuberculate appearance to the surface, with serrate or toothed edges; testa crustaceous; kernel whitish, fleshy; embryo small, in fleshy endosperm; odor very little; taste bitter, afterward biting and acrid.

## DIOSCOREA.

Dioscorea. Wild Yam Root.

1. The dried rhizome of *Dioscorea villosa* Linné (Fam. *Dioscoreaceae*).

2. Knotted and woody, elongated, sparingly branched, 6 to 12 mm. thick, somewhat compressed, bearing scattered nodular projections at the sides, elongated, slender tough roots underneath and stem-scars on the upper surface; pale brown, surface more or less scaly from the partly detached thin outer layer; fracture short but not weak, the fractured surface whitish or pale-brown, with numerous small wood bundles; odorless; taste starchy and slightly acrid.

## FRAXINUS.

White Ash Bark.

1. The dried bark, deprived of the corky layer, of the trunk of *Fraxinus Americana* Linné (Fam. *Oleaceae*) and probably of other species of Fraxinus.

2. In flat pieces of varying length and width 3–6 mm. thick; externally yellowish or pale brown, sometimes with ridges of a warty nature and fissures of a grayish-brown color with markings of lichens; inner surface, pale brown to yellowish, striate; fracture very uneven, somewhat fibrous; odor faintly aromatic; taste bitter, weakly acrid.

3. Ash not over 10 percent.

## FRUCTUS RUBI.

Blackberry.

1. The fresh ripe fruit of varieties of *Rubus nigrobaccus*, Bailey, or *Rubus villosus* Aiton (Fam. *Rosaceae*).

2. An aggregate fruit, ovate to oblong-rounded or slightly pointed, composed of numerous shining black drupelets attached to an esculent receptacle; pericarps externally smooth or with only a few hairs (R. villosus); mesocarps fleshy, juice purple-red; endocarps hard, black, surfaces deeply wrinkled; taste sweet and slightly acid.

## FRUCTUS RUBI IDAEI.

Raspberry.

1. The fresh ripe fruit of varieties of *Rubus Idaeus* Linné (Fam. *Rosaceae*).

2. An aggregate fruit, globular or hemispherical with a concave depression at the base where separated from the receptacle, composed of twenty or more small rounded polygonal succulent drupelets; pericarps externally red, hairs numerous; mesocarps fleshy, juice red; endocarps small stones with wrinkled surfaces; odor characteristic, aromatic; taste pleasant, sweet, acidulous.

3. For pharmaceutical purposes, the black raspberry, the fresh ripe fruit of cultivated varieties of Rubus occidentalis Linné (Fam. *Rosaceae*) may be used either in part or entirely in place of the red raspberry.

## FRUCTUS SOLANI CAROLINENSIS.

Horse-nettle Berry.

1. The air dried ripe fruit of *Solanum Carolinense* Linné (Fam. *Solanaceae*).

2. Globose, slightly depressed and somewhat shriveled and wrinkled in drying .8 to 2 cm. in diameter, orange-yellow, glabrous, fleshy, two-celled, many-seeded, calyx and pedicle usually persistent; calyx stellate-pubescent, deeply five-lobed, the lobes ovate or ovate-lanceolate, acuminate and enclosing half or more of the berry; seeds orbicular, flat, yellow, smooth shining; odor pepper-like; taste bitter and acrid.

3. Ash about 5 percent.

## GEMMAE POPULI.

Balsam Poplar Buds. Balm of Gilead Buds.

1 The air dried closed winter leaf buds of *Populus nigra* Linné and *Populus balsamifera* Linné (Fam. *Salicaceae*), collected early in the spring. Balsam poplar buds should be kept in tightly closed containers of glass or tin.

2. Conical, pointed, up to 2 cm. long and 2 to 5 mm. thick, consisting of closely imbricated scales, externally brown and glossy, glutinous with fragrant resin; odor pleasant, balsamic; taste aromatic, bitter.

## JUGLANS.

Juglans. Butternut Bark.

1. The dried bark of the root of *Juglans cinerea* Linné (Fam. *Juglandaceae*) collected in autumn.

2. In quills, curved strips or chip-like pieces 3 to 10 mm. thick; deep chocolate-

brown color on both surfaces and throughout, except for the faint intersecting whitish radial and tangential lines seen on transverse section; outer surface smoothish or somewhat warty, the inner bearing fragments of adhering thin stringy fiber; fracture short, rather weak, slightly fibrous; taste faintly aromatic, bitter, somewhat pungent and acrid.

## JUNIPERUS.

### Juniper Berries.

1. The carefully dried ripe fruit of *Juniperus communis* Linné (Fam. *Coniferae*). Juniper berries should be kept in air-tight tin or glass containers. Old or insect-infected fruit should not be used.

2. Nearly globular, about 8 mm. in diameter; externally smooth, shining black-brown to purplish-black with a blue-gray bloom, at the apex a three rayed furrow marks the cohesion of the three fleshy bracts forming the pericarp; internally loosely fleshy, greenish-brown, containing numerous large schizogenous cavities; seeds three, triangular ovate, hard, brown, with large uneven oil glands on the surface; odor aromatic; taste sweet, pleasant, terebinthinate, slightly bitter.

3. Ash not more than 5 percent.

4. Sections examined under the microscope exhibit a pericarp consisting of an epiderm of a single row of rounded polygonal cells filled with a brown granular substance, at the sutures of the bracts these become blunt papillae, a hypoderm of 2 or 3 rows of brown-red, wide collenchyma thickened at the angles; the fleshy portion (mesophyl) composed of loose irregular parenchyma with large oval canals and traversed by fibro-vascular bundles with areolated fibers; a sclerenchymatous ring of 6 to 8 rows of very thick cells with pitted walls many enclosing prismatic crystals of calcium oxalate; the seed-testa shows a layer of 2 to 10 rows of stone cells with radial markings on the walls and each enclosing a polygonal crystal of calcium oxalate; endosperm and embryo rich in fat and aleurone.

## LAC VACCINUM.

### Cow's Milk.

The fresh whole milk, complying with the legal standard, of the domestic cow *Bos taurus* Linné (Fam. *Bovidae.*)

## MENYANTHES.

### Menyanthes Leaves.

### Buckbean. Marsh Trefoil.

1. The dried leaves of *Menyanthes trifoliata* Linné (Fam. *Menyanthaceae*).

2. Glabrous; petioles 10 to 15 cm. long, stout but soft and weak, the base more or less sheathed with broad, thin and membranaceous, somewhat translucent stipules; blade ash-green, trifoliate; leaflets sessile or very short-petioled 5 to 8 cm. long and usually about two-thirds as broad, obovate, blunt, entire or occasionally coarsely and unequally crenate; odor slight but characteristic; taste decidedly bitter.

3. Ash not more than 10 percent.

## OLEUM AURANTII AMARI CORTICIS.

### Oil of Bitter Orange Peel.

1. A volatile oil obtained by expression from the fresh peel of the Bitter Orange, *Citrus Aurantium* Linné *subspecies amara* Linné (Fam. *Rutaceae*). It should be kept in small amber-colored well-stoppered bottles, in a cool place. Oil that has developed a terebinthinate odor should not be dispensed.

2. A pale yellow liquid, having the characteristic, aromatic odor of orange and an aromatic somewhat bitter taste.

3. Soluble in four volumes of Alcohol, the solution should be neutral to litmus paper; also soluble in all proportions in Absolute Alcohol and in an equal volume of Glacial Acetic Acid.

4. Specific gravity: 0.846 to 0.854 at 25° C.

5. Its optical rotation dextrogyrate from 92° to 94° in a 100 mm. tube at 25° C.

6. Introduce 50 cc. of Oil of Bitter Orange Peel into a 200 cc. three bulb, fractionating flask. Distil the oil at the rate of 2 cc. per minute until 5 cc. of distillate has been collected. The angle of rotation of this distillate of 10 percent of the oil, should be equal to or slightly higher than that of the sample before distillation.

## OLEUM AURANTII FLORUM.

### Oil of Orange Flowers. Oil of Neroli.

1. A volatile oil distilled from the fresh flowers of the Bitter Orange, *Citrus Aurantium* Linné *subspecies amara* Linné (*Citrus vulgaris* Risso, *Citrus Bigaradia* Risso) (Fam. *Rutaceae*). It should be kept in small amber-colored well-stoppered bottles in a cool place, protected from light.

2. A pale yellow, slightly fluorescent, neut-

ral liquid, having the fragrant odor of orange blossoms and an aromatic, at first sweet then somewhat bitter taste.

3. Specific gravity: 0.868 to 0.875 at 25° C. Optical rotation is dextrogyrate from 1° 30′ to 5° in a 100 mm. tube at 25° C.

4. Shaken with a concentrated solution of sodium bisulphate it assumes a permanent purple-red color.

5. Soluble in an equal volume of Alcohol, the solution having a violet fluorescence and a neutral reaction to litmus paper. Soluble in 2 volumes of 80 percent Alcohol, the solution becoming cloudy on further addition of Alcohol of same percentage.

## OLEUM BERGAMOTTAE.

Oil of Bergamot.

1. A volatile oil obtained by expression from the rind of the fresh fruit of *Citrus Bergamia* Risso (Fam. *Rutaceae*). It should be kept in small amber-colored well-stoppered bottles in a cool place, protected from light.

2. A green or greenish-yellow liquid, neutral or only faintly acid, having a characteristic fragrant odor and a bitter taste.

3. Specific gravity: 0.875 to 0.880 at 25° C. Optical rotation dextrogyrate from 8° to 24° in a 100 mm. tube at 25° C.

4. Two volumes of the Oil, when mixed with one volume of Alcohol, should give a clear solution and this should not become turbid on the further addition of Alcohol. Soluble in two volumes of 80 percent Alcohol with not more than a slight cloudiness and no separation of oil globules. Soluble in all proportions in Glacial Acetic Acid.

5. If a weighed portion, about 2 gm. of the Oil be evaporated in a tared dish, on a water-bath, until the odor has completely disappeared, a soft green, homogeneous residue should be left, amounting to not more than 6 percent of the Oil (fixed oils).

6. To 2 gm. of Oil of Bergamot add 10 cc. of alcoholic potassium hydroxide, V. S., evaporate to dryness and incinerate. Extract the ash with water and acidify with diluted nitric acid, no cloudiness should be produced on addition of silver nitrate T. S. (Chlorinated Compounds).

7. To 2 gm. of Oil of Bergamot add 20 cc. of half-normal alcoholic potassium hydroxide V. S. and heat the mixture in a flask on a water-bath filled with boiling water under a reflux condenser for a half hour. Cool the mixture and add 100 cc. Distilled Water and titrate with half-normal sulphuric acid V. S., using phenolphthalein as indicator, not more than 12.6 cc. of acid should be required, indicating a minimum content of 36 percent of ester, calculated as linalyl acetate, in the oil.

## OLEUM MYRCIAE.

Oil of Myrcia. Oil of Bay.

1. A volatile oil distilled from the leaves of *Pimenta acris* Wight (Fam. *Myrtaceae*). It should be kept in small well-stoppered amber-colored bottles, in a cool place, protected from light.

2. A yellow or brownish-yellow liquid having a pleasant aromatic odor and a pungent spicy taste.

3. Specific gravity: 0.965 to 0.985 at 25° C. Optical rotation lævorotatory from 2° to 6° in a 100 mm. tube.

4. With an equal volume of Alcohol, Glacial Acetic Acid, or Carbon Disulphide, it yields slightly turbid solutions. The alcoholic solution is slightly acid to litmus paper.

5. When mixed with an equal volume of a concentrated solution of sodium hydrate, it forms a semi-solid mass.

6. If 2 drops of the Oil be dissolved in 4 cc. of alcohol, and a drop of ferric chloride T. S. be added, a light green color will be produced; and if the same test be made with a drop of diluted ferric chloride T. S., prepared by diluting the test solution with four times its volume of water, a light bluish coloration will be produced, which soon disappears.

7. To 3 drops of the Oil, contained in a small test-tube, add 3 drops of sulphuric acid, cork the test-tube and allow the mixture to stand for half an hour, a resinous mass should be obtained. On adding to this mass 4 cc. of diluted alcohol, vigorously shaking the mixture, and gradually heating on a water-bath to the boiling point, the liquid should remain nearly colorless, and should not acquire a red or purplish-red color (distinction from oil of pimenta and oil of cloves).

8. Shake 1 cc. of the Oil with 20 cc. of hot water, the water should not give more than a scarcely perceptible acid reaction with litmus paper.

9. If, after cooling, the liquid in the test above be passed through a wet filter, the clear filtrate should produce, with a drop of ferric

chloride T. S., only a transient grayish-green, but not a blue or violet, color (absence of phenol).

## OVUM GALLINACEUM.

Hen's Egg.

The recently laid egg of the hen *Gallus domesticus* Temminck (Fam. *Phasianideae*).

## PASSIFLORA.

Passion Flower. Passion Vine.

1. The dried herbage of *Passiflora incarnata* Linné (Fam. *Passifloraceae*) collected after some of the berries have matured.

2. Stems glabrous or slightly pubescent above, striate, 6 to 8 mm. in diameter, of variable length, woody, hollow, the cavity about one-half the diameter; bark very thin, greenish or purplish; wood very porous and bordered on the inner side by a thin layer of pith; fracture uneven, of the stem smooth, of the bark coarsely fibrous.

3. Leaves more or less broken in drying, rather thick, glabrous or often pubescent, nearly orbicular in outline, base cordate, deeply 3 to 5 lobed, lobes ovate, acute, finely serrate, petioles 1 to 5 cm. long with 2 glands near the summit. Tendrils numerous and closely coiled.

4. Flowers solitary, axillary, peduncles as long as the petioles, usually 3 bracted; calyx cup-shaped 4-5 lobes, lobes linear, imbricated, cuspidate, corona purplish; petals 4-5 dirty yellow; ovary oblong, stalked; stamens monadelphous in a tube about the stalk of the ovary, separated above, anthers narrow, versatile.

5. Fruit 4 to 5 cm. long, an ovid many-seeded berry; externally green or yellow, shriveled and wrinkled; seeds flat, ovate, yellowish to brown arilled.

6. Taste and odor slight.

7. Ash not over 12 percent.

## PUMEX.

Pumice.

1. A substance of volcanic origin, consisting chiefly of complex silicates of aluminum, potassium and sodium.

2. Very light, hard, rough, porous gray masses or a gritty, gray-colored powder.

3. Permanent in the air, odorless and tasteless. The dry masses usually float on water.

4. Boil 10 gm. of Pumice with 50 cc. distilled water for one-half hour, adding water from time to time to maintain approximately the original volume and filter; the filtrate should be neutral to litmus paper, and one-half of this filtrate when evaporated and dried at 110° C. should yield not more than 0.01 gm. residue (*limit of soluble substances*). The remaining half of the filtrate after slightly acidulating with hydrochloric acid should not yield a blue color with Potassium Ferrocyanide T. S. (absence of *iron*).

5. Boil 1 gm. with 25 cc. diluted hydrochloric acid for one-half hour, adding water from time to time to maintain approximately the original volume, then filter the liquid; the filtrate should yield upon evaporating to dryness, igniting and quickly weighing, not more than 0.05 gm. of residue.

## SAMBUCUS.

Sambucus. Elder Flowers.

1. The air dried flowers of *Sambucus canadensis* Linné or of *Sambucus nigra* Linné (Fam. *Caprifoliaceae*) separated from the peduncles and pedicels.

2. Small, about 2 to 3 mm. broad, shriveled; calyx superior, five lobed; corolla cream colored to brownish-yellow, rotate, flat or slightly campanulate, regularly five lobed; stamens five inserted at the base of the corolla and alternating with its lobes, filaments slender, anthers oblong, yellow; pollen ellipsoidal or tetrahedral and rounded, covered with finely punctate markings and three parallel longitudinal slits; taste slightly bitter; odor faintly sweet and aromatic.

3. Ash white and not more than 8 percent.

## SENECIO.

Senecio. Life Root.

1. The dried overground portions of *Senecio aureus* Linné (Fam. *Compositae*) gathered when flowering.

2. Stems 3 to 6 dm. long, if entire bearing a basal rosette of leaves; sparingly clothed with successively smaller leaves and bearing at the summit several yellow heads in a loose corymb, white floccose when young, but mostly glabrous when in flower; radical leaves on long slender petioles, mostly of rounded form 5 to 7 cm. broad, the base often cordate, the summit rounded, the margin crenate-dentate; stem-leaves gradually changing from the shape of the radical leaves to lyrately pinnate, then pinnatifid and sessile, and at length clasping, oblong and incised; heads slender peduncled, 12 to 25 mm. broad, the lance-linear involucral scales in about 2 series, closely appressed, rays about 10,

bright-yellow, disk flowers very numerous, small, bearing a glabrous akene and a white pappus; odor characteristically aromatic; taste bitter, slightly astringent and distinctly acrid and pungent.

## STRONTII CARBONAS.

### Strontium Carbonate.

1. It should contain at least 99 percent of Strontium Carbonate ($Sr\ CO_3 = 147.62$).

2. A white powder, odorless and tasteless.

3. Insoluble in water, soluble with effervescence in diluted hydrochloric, nitric or acetic acids. Addition of diluted sulphuric acid to these solutions produces a white precipitate.

4. 1 gm. should yield a clear solution with 10 cc. of diluted hydrochloric acid (*sulphate*).

5. 10 cc. of a 1:100 solution, solution being effected by a slight excess of nitric acid added to the water, should not become more than slightly opalescent at once on adding silver nitrate T. S. (limit of *chloride*).

6. Dissolve 1 gm. in water by means of a slight excess of acetic acid, and dilute to 100 cc. On adding to 10 cc. of this solution 5 drops of potassium dichromate T. S. no turbidity should develop within five minutes (limit of *barium*).

7. .5 gm. dissolved in diluted hydrochloric acid should not respond to the U. S. P. Time Limit Test for *heavy metals*.

8. Shake 2 gm. with 25 cc. of water and filter, on evaporation of the filtrate and drying the residue at 100° C. it should weigh not more than 0.01 gm. (limit of *soluble substances*).

9. Dissolve about 1.5 gm. (accurately weighed) in 30 cc. of hydrochloric acid V. S. and titrate the excess of acid with sodium hydroxide V. S., using methyl orange as indicator. Each cc. of normal acid consumed is equivalent to 0.07381 gm. strontium carbonate.

## SUCCUS CITRI.

### Lime Juice.

1. The expressed juice of the ripe fruit of *Citrus medica, var. acida* Linné (Fam. *Rutaceae*). 100 cc. should contain from 5 to 10 gm. of total acids, calculated as crystallized citric acid.

2. A clear or slightly turbid, pale yellow or yellowish-green liquid, having the characteristic odor and taste of limes.

3. Specific gravity: 1.025 to 1.040 at 25° C.

4. To 5 cc. of Lime Juice add 20 cc. solution of potassium hydroxide and heat in a 100 cc. flask together with 0.5 gm. of granular aluminum or aluminum foil on a water bath for 10 minutes, no odor of ammonia should be noticeable at any time during the heating (absence of *nitrates*).

5. If .1 cc. of barium chloride T. S. be added to 5 cc. of clear filtered Lime Juice, only a slight turbidity should be produced after standing two minutes (limit of *sulphates*).

6. If .1 cc. of nitric acid followed by .1 cc. of silver nitrate T. S. be added to 5 cc. clear filtered Lime Juice, only a slight opalescence should be produced after standing two minutes (limit of *chlorides*).

7. If 5 cc. each of sulphuric acid, alcohol and Lime Juice be heated, no odor of acetic ether should be developed (limit of *acetates*).

8. Add 1 cc. of an aqueous solution of potassium acetate (1 to 3) to 5 cc. of filtered Lime Juice and then add to the mixture alcohol in excess, a slight cloudiness may occur but no crystalline precipitate should be formed within 15 minutes (limit of *tartrates*).

9. Upon evaporation and ignition until free from carbon, Lime Juice should not leave more than 0.5 percent of ash. The ash from 5 cc. of lime juice when dissolved in a few drops of nitric acid and diluted with water should show not more than traces of phosphate when tested with ammonium molybdate T. S.

10. Lime Juice should contain not more than 0.04 percent of sulphurous acid ($SO_2$) when tested by the method of the U. S. P. IX Revision for determining $SO_2$ in gelatin.

11. Upon distilling 200 cc. of Lime Juice with excess of calcium hydroxide until 100 cc. of distillate is obtained, the specific gravity of the distillate should indicate not more than 2 percent of absolute alcohol by volume in the distillate or 1 percent in the lime juice (limit of *alcohol*).

12. Shake 10 cc. of Lime Juice acidified with sulphuric acid with 25 cc. of ether, separate the ether and evaporate it to dryness, the residue should not be crystalline and, when dissolved in about 3 cc. of water, should not produce a purplish color on addition of one drop of ferric chloride T. S. (*salicylic acid*).

13. Shake 10 cc. of Lime Juice acidified with sulphuric acid with 25 cc. of ether and

separate the ether and evaporate it to dryness, the residue should not be crystalline and, when dissolved in 3 cc. of water and carefully neutralized with ammonia water, should not produce a flesh colored precipitate on the addition of one drop of ferric chloride T. S. (*benzoic acid*).

14. Dilute 20 cc. of Lime Juice with 100 cc. of water, filter, if necessary, and add 4 cc. of diluted hydrochloric acid. Into this solution immerse a piece of wool which has been boiled in a very dilute solution of potassium hydroxide T. S. and then washed in water, and boil for 5 to 10 minutes. Remove the wool, wash thoroughly in water, and boil in a very dilute solution of hydrochloric acid. After washing out the acid with water, boil with about 200 cc. of 2 percent solution of ammonium hydroxide until the color on the wool, if any, is dissolved. Remove the wool, and add a slight excess of hydrochloric acid to the solution. Immerse in this solution another piece of wool which has been treated with potassium hydroxide solution in the same manner as the first. Boil. This second piece of wool should not be dyed (*aniline dyes*).

## SUCCUS POMORUM.

Fresh Apple Juice.

The freshly expressed juice of sound, ripe, sour apples, the fruit of cultivated varieties of *Pyrus malus* Linné (Fam. *Rosaceae*).

## TRIFOLIUM.

Trifolium. Red Clover Blossoms.

1. The dried flowering heads of *Trifolium pratense* Linné (Fam. *Leguminosae*).

2. Heads ovoid with rounded summit, mostly 12 to 25 mm. long and broad, shriveled, purplish and more or less brown from drying, consisting of many small papilionaceous flowers, crowded together and clothed at the base with broad, pointed, ciliate stipules of a pale green color with darker veins, and which may or may not be accompanied by diminutive trifoliolate leaves. Flowers 12 to 15 mm. long; calyx about two-thirds the length of the corolla, the pilose campanulate tube a little longer than the four short nearly equal teeth and shorter than the narrower fifth one, calyx-teeth subulate, tapering; petals united into a tube below, the standard longer than the wings but when recurved appears shorter; stamens diadelphous (9 and 1); style slender; odor faintly aromatic and somewhat tea-like; taste sweetish, then slightly bitter.

## TRILLIUM.

Beth Root.

1. The dried rhizome of *Trillium erectum* Linné (Fam. *Liliaceae*) and closely allied species of *Trillium*.

2. Rhizome oblique, globular, oblong or obconic, truncate below, terminated by a small bud surrounded by a sheath of scarious leaf bases, annulated by leaf scars and fissured by stem scars; .6 to 2.5 cm. wide by .6 to 5 cm. long, more or less compressed laterally, rootlet scars in several concentric rows on the under side in the upper portions; externally yellowish to reddish-brown; internally of a pale yellow; fracture somewhat uneven with a more or less spongy appearance; odor distinct; taste bitter and acrid with a sensation of warmth in the throat and when chewed causing an increased flow of saliva.

3. Ash not more than 5 percent.

## VERBENA.

Verbena. Blue Vervain.

1. The dried overground portion of *Verbena hastata* Linné (Fam. *Verbenaceae*) collected when flowering.

2. In broken or cut pieces of stout, obtusely quadrangular stems which bear opposite leaves and terminal interrupted panicles of spikes of blue flowers; rough, hairy throughout, except the corolla, the tube of which is externally pubescent; petioles 12 to 25 mm. long; leaves 6 to 12 cm. long, lanceolate, acuminate and acute, coarsely and sharply serrate, or the lower hastately lobed, deep green above, paler beneath, conspicuously veined; spikes erect, cylindraceous, densely flowered, each flower subtended by a lanceolate acute bract; calyx adherent, a little more than half the length of the corolla, tubular, 5 lobed, the mouth slightly oblique; corolla small, bright blue, salver-form, sub-equally 5 lobed; stamens adnate to the corolla tube, included, didynamous; fruit dividing at maturity into four one-seeded parts; odor heavy, especially if dampened; taste bitter and disagreeable.

## VITELLUM OVI RECENS.

Fresh Egg Yolk.

The freshly separated yolk of recently laid eggs of the hen *Gallus domesticus* Temminck (Fam. *Phasianidae*.)

## Of General Interest

### CALIFORNIA; 1915!

Representatives from the various branches of the pharmaceutical profession located in and about San Francisco met in enthusiastic conference in that city on the evening of April 20, to take preliminary steps toward the entertainment of the members of the profession who will be in attendance upon the various meetings of the craft which are to be held in that city during the maintenance of the Panama Pacific Exposition. An organization was effected with Mr. J. A. Sanford, the President of the California Pharmaceutical Association, as chairman. The meeting was addressed by Mr. James A. Barr, Chief of the Bureau of Conventions and Societies for the Exposition, who told of the painstaking work of his department, in planning for the proper accommodation of the many associations, who are to have their meetings at the Golden Gate during the fair.

Mr. Fred I. Lackenbach spoke of the warm responses which he had received, from all sources, to his suggestion that the A. Ph. A. hold its meeting in San Francisco in 1915. Addresses were made by several other gentlemen, in support of Mr. Lackenbach's proposition, and the meeting voted to appoint a committee of three to "work out" the details of plans for the accommodations of the members of the profession who attend the fair.

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### A SYMPOSIUM ON THE PROPOSED HARRISON BILL.

At the meeting of the Philadelphia Branch of the A. Ph. A., a number of letters were read on the subject of the so-called Harrison Bill, now pending in the U. S. Senate, and in view of the grave importance of the provisions of this bill to the pharmacists of the country, we give space to print these letters in the columns of the JOURNAL, trusting that a full and frank discussion of the matter will redound to the advantage of the profession.

Washington, D. C., May 4, 1914.

Dear Prof. Cook:

With reference to the so-called Harrison Bill and the misunderstanding of same by many retail pharmacists, permit me to discuss the question briefly and to say that this is largely due to their misconception of the necessity for such legislation by the Federal Government and also their lack of understanding of the provisions of the pending measure and what it is intended to accomplish.

The necessity for the so-called Harrison Bill was not made manifest by the medical profession, drug trade or any of its allied branches. It was the result of careful study, after due investigation, by Federal officers, covering a period of several years, into the evils of drug addiction all over the United States. The appalling conditions unearthed in Philadelphia and other large cities, where school children of tender age had contracted the drug habit, and the fact that a large majority of crimes the past ten years, and especially in the South, were directly traceable to the habitual use of narcotic drugs, led the Federal Government, through its officers, to originally draft a bill which had for its object the absolute control of narcotic drugs, so that they could be sold and used for medicinal purposes only.

This bill being so drastic in its provisions, and the knowledge that, if passed, it would cause no end of trouble for those who of necessity would be required to handle such drugs, led the American Pharmaceutical Association to consider the proposition and to suggest the advisability of the formation of a Conference, whereby all affected interests could come together on common ground, discuss the question and agree upon something feasible yet effective, that would not be unworkable nor prove a burden and at the same time would carry out the original object, the proper protection of the public. It therefore then is a public health measure, and not one, as some seem to think, which will grant special privileges to certain classes.

The American Pharmaceutical Association, in bringing together the Conference, acted with the noblest of objects in view, the welfare of the public, yet at the same time they have conserved the interests of the retail pharmacists as far as possible and have succeeded in removing what would have been a burden, namely, the keeping of records of all

sales of narcotic drugs and the making of returns of the same. * * *

(Then follows a brief review of the field covered by the bill as already printed.—ED.)

By comparing the sections of the amended "Harrison Bill" with the bill as originally proposed, it will be seen that the burdensome task of keeping a record of all sales of narcotic drugs and annually making returns of same, has been eliminated through the efforts of the National Drug Trade Conference, that was organized through the efforts of the American Pharmaceutical Association, and instead, records of purchases are provided for and returns are to be made only when demanded. Is not this work of the American Pharmaceutical Association to be commended and has not the organization conserved the welfare and interests of the retail pharmacists?

As this is a revenue measure it will require all dealers to obtain a license and further provides that the duplicate order blank shall be purchased from the collector of internal revenue, the license-fee is small and the price of the blanks nominal, so that while it is a revenue measure, it will furnish revenue sufficient only to properly carry the act and its enforcement.

With this act in operation and the coöperation provided whereby the present state officials can obtain information necessary for the enforcement of state laws, it will then become unnecessary for the various states to enact new laws, present state laws being quite sufficient if enforced; if not, they can be amended.

The enforcement of present state laws, with this act in operation, will reduce illicit traffic in narcotic drugs to the minimum. That is all that is expected, and it therefore then should receive the support of every self-respecting retail pharmacist in the United States.

A careful study of the provisions of this proposed act leads me to point out that the legitimate retail pharmacist will have but few burdens thrust upon him by its enactment into law, and that the necessary extra labor entailed will be more than compensated for by the good he will do toward humanity, preventing future drug-addiction, overcome the wrecking of individuals and homes and the prevention of crimes, consequently I believe every effort should be put forth to assist in securing the passage of the bill, thereby cleaning out the dope-sellers and at the same time assist in placing our calling in the position to which it is entitled and where it will be more respected.

Sincerely yours,

S. L. HILTON.

April 30, 1914.

My Dear Professor Cook:

I am pleased, indeed, to learn that the Philadelphia Branch of the American Pharmaceutical Association is to discuss the so-called "Harrison Bill" and its relation to the retail drug trade. It appears somewhat unfortunate that drug associations in various parts of the country have not discussed this proposed legislation in as temperate and as thorough a manner as might have been done if more accurate information regarding the object and scope of the proposed legislation had been presented.

The so-called Harrison Anti-Narcotic Bill, usually referred to as "H. R. 6282," cannot in any sense be considered a regulatory measure and will at best only secure for state and local officials the necessary information to make existing laws operative. This information is to be secured by utilizing the taxing power of the Federal Government in such a way as to impose a nominal license-fee on all who are in any way engaged in the sale or distribution of certain enumerated drugs. In addition to the license-fee, the law also requires that all sales of the enumerated drugs be recorded in a specific way, the method outlined being designed to impose the minimum of trouble to the dealer and to secure the maximum information for officials entrusted with the enforcement of Federal, state or municipal laws and regulations.

How essentially necessary authentic sources of information really are, to enforce local laws, has been amply shown in the state of Pennsylvania, in connection with the cocaine law, and has been further emphasized in the state of New York, where the recently enacted Walker cocaine law was found to be quite inoperative because of the promiscuous introduction of cocaine from without the state, and the development of the illicit traffic by peddlers and others in no way connected with legitimate drug business.

That much misleading information has been published from time to time in regard to the extent of the abuse of narcotic drugs must

be admitted, but from the retail pharmacist's point of view, the opposition that has been evidenced to the enactment of the Harrison Bill has been altogether unfortunate, in that the public at large has been misled into interpreting this opposition as a justification of the frequently-made charge that retail druggists and men connected with the drug business generally, are primarily to blame for the very widespread misuse of opium and coca, their alkaloids and derivatives. It is for this latter reason alone, that it appears altogether unfortunate that the members of the drug trade have evidenced any, even passive objection, to the enactment of the Harrison Anti-Narcotic Bill, as adopted by the House of Representatives last June. The adoption of the various amendments that have been offered to the Committee on Finance of the Senate, and more recently in the Senate itself, do not in any way improve the measure as a source of information, and if embodied in the law as finally enacted, would serve to increase, unnecessarily, the difficulties of enforcing the law without securing any reasonable amount of additional information for the benefit of persons entrusted with the enforcement of local regulatory measures.

From the point of view of the retail druggists and members of the drug trade generally, it would appear desirable to endorse any reasonable legislation that will secure the necessary information to clearly place the onus of the drug abuse where it rightfully belongs, and if it should develop that members of the drug trade are to blame for the promiscuous use of drugs of this type, druggists themselves should be the first to insist that the continuation of such abuse be corrected by additional legislation, and thus clearly show that the promiscuous distribution of habit-forming drugs is not recognized in any way as being a part of the legitimate traffic in drugs and remedial agents.

Very truly yours,

M. I. WILBERT.

My Dear Professor Cook:

Mr. White has handed me your letter of April 29, 1914, with the request that as Counsel for the N. A. R. D. that I answer the same.

In reply I have to say that should the Harrison Bill be so drafted so as to include all parties handling narcotics, and place them under regulations, which will apply with equal force to all alike, it will be of the greatest benefit. But should this bill pass in a shape so that it will apply unequally to the different classes of people who handle narcotics, it will not only be inefficacious, but it will create such bad feeling and friction as will make its enforcement well nigh impossible.

When Mr. Henry of your city was here I took pains to explain this situation to him and he no doubt will be glad to furnish you any details regarding the legislation.

Yours very truly,

ALONZO H. STEWART.

Dear Dr. Cook:

It gives me a real pleasure to discuss the so-called "Harrison Bill" for consideration by the Philadelphia Branch, and in doing so, I am not unmindful of the fact, that my views regarding the merits of the so-called "Harrison Bill" differ or at least have differed on some vital points from the views as held by two members of the Philadelphia Branch who are also members of the National Drug Trade Conference, and I must take it somewhat for granted, that the views held by said members of the Philadelphia Branch are largely the views of the Branch membership. In this connection I feel called upon to say, that I have always approached the subject as much as possible from the view point of the retail pharmacist seeking to serve best the public need and welfare.

You request a brief contribution, and briefness will be my endeavor, though I must point out, that the many important features will permit brevity only at the expense of clearness and adequacy. The discussion as you say is to be on the so-called "Harrison Bill," in its amended form as now before the Senate, and I take this to mean "H. R. 6282, Calendar No. 213."

The Harrison Bill, in its present form represents an exercise of the taxing power of the Federal Government, and is incidentally only an exercise of its control over interstate commerce, all for the purpose of providing necessary regulation for the distribution of narcotics, which the several states are either unable or unwilling to provide, and frequently indifferent to enforce, in so far as they can provide them. The taxing power is exercised nominally only, not so much with a view of yielding revenue, as with a view of affording a constitutional ground for Federal activity. Constitutional limitations will

not permit the Federal Government to prescribe in direct terms who may or may not sell or distribute within the several states, but to a large extent this can be accomplished by indirection based upon state legislation. On that account a proper Federal law will need to give every person the right to pay the proposed tax, and thus become registered as a dealer in narcotics. Now it may be argued, that under the circumstances the requirement for a $1.00 tax which all can pay, will not be very helpful, because any drug fiend will gladly pay such a tax of $1.00 to secure the right of purchase and possession, by becoming a dealer, and then simply supply his personal wants. However, the Harrison Bill, as drafted, gives the Commissioner of Internal Revenue with the approval of the Secretary of the Treasury, the right to make needful rules and regulations, for carrying out the provisions of the Act, and this authority would seem to be wide enough to prescribe such regulations as will successfully limit the right to become registered as a dealer, to such persons who in fact are dealers, so that there would be but little danger that one who intends merely to be a consumer, could secure the right of possession as a registered dealer. This feature might possibly have been strengthened, but to attempt to do so may not have been expedient. Assuming, that, under this requirement, the right of possession for further distribution can be successfully limited to actual dealers, it must be granted, that, to this point, nothing more has been secured but what already exists, because the supply of narcotics for illegitimate use to-day comes from dealers of some sort, and there is no need evidently at present, for illegitimate users to become nominally dealers. It follows, that whatever benefit we are to secure from the proposed Federal legislation, must depend upon the greater restrictions which are placed upon the present dealers, most of whom we must assume will be entitled to registration under the intended Act. It is here, where the authority and power of the Federal Government is dependent entirely upon what it may not do directly, but what it may do to a large extent by indirection. To accomplish by indirection what the Federal Government may not do directly, there has been adopted a record system which has been embodied in the Harrison Bill, and, presumably, for the proper enforcement of a revenue measure the distribution is required to be evidenced by a record of some sort. If this requirement for a record were made applicable to every distribution a large measure of success would seem to be assured. The entire frame work of the Harrison Bill contemplates that the drugs may reach the consumer only through sources, which by state law are authorized to alone supply the consumer for legitimate purposes. This result is secured by making all other distribution dependent upon having an Official Order Form, which of course can be had only by registered dealers. Since the entire narcotic evil ultimately comes from the traffic, which reaches the consumer, the all important question is, whether the control sought to be secured by indirection is sufficient in that respect. If the control over the drug and its distribution to the consumer, is incomplete or insufficient, then the entire proposed legislation is condemned to failure, for every other feature of the bill is merely an incident to the ultimate aim of limiting distribution entirely to legitimate final use and consumption. As already stated, the success of the Federal Act in limiting consumption of the drug to legitimate purposes is greatly dependent upon existing proper state legislation, always provided of course, that the control and supervision sought by indirection, through record requirement, is made uniformly applicable, so as to reach every case in which the drug is distributed for consumption. In my opinion, generally speaking, existing state laws are sufficient to act as a basis upon which indirect Federal control can be built. To me it seems, that the sufficiency of the Harrison Bill is therefore dependent upon the question of whether it aims to be uniformly applicable. Not considering at this point preparations which contain minimum quantities and which are exempted, the Harrison Bill if otherwise so drawn as to be enforcible, will because of the record requirement, limit successfully all distribution by retail pharmacists to consumers on prescriptions exclusively, and thus this source of supply for the consumer will be restricted to legitimate use. The bill requires with one unfortunate exception, that every distribution to the consumer be evidenced by a record in the form of a physician's prescription. Since the right to write prescriptions is limited throughout to certain classes, who are licensed to do so under state law, and since the right to fill prescriptions is limited to an-

other class licensed by state law, it would appear, that by making a record requirement in the form of prescriptions, one source of supply to the consumer will be sufficiently safeguarded. Up to this point the provisions of the Harrison Bill command utmost respect. Right at this point it fails, and, if unchanged, it will be largely a useless measure representing an enormous waste of time, energy and trouble. By Sub-section (a) of Section II, of the Harrison Bill, as advocated by the National Drug Trade Conference, and as contained therein, altogether because of the action of said conference, the distribution by physicians, dentists and veterinarians to the consumer are to be altogether without the need for record requirement. Under the bill a physician, dentist or veterinarian may distribute ten ounces of cocaine during a day and not be required to show what he has done with them, further than to say, that he has used them in the course of his professional practice. The fundamental idea of the Harrison Bill, is to control the existing evil by means of a system of record keeping. We may assume, or at least hope, that this would be largely successful, but the fundamental idea is not carried through to a logical conclusion, and while the law contemplates that the consumer may secure narcotics from about two hundred and fifty thousand physicians, dentists, veterinarians and pharmacists, it would enforce the fundamental idea with which success is hoped for, as against only less than fifty thousand, and would ignore it altogether with reference to the other, about two hundred thousand. If the fundamental idea underlying this proposed legislation means success, if uniformly carried out, it must be doomed to failure if applied to only one-fifth of those to whom it then should apply.

It has always been, and is now, my judgment that the physician, dentist or veterinarian, who would assume the functions of a pharmacist, should be governed by the exact same legal requirements and restrictions. It is my contention that the illegitimate traffic in narcotics is not by any means confined to possible wrong doers who are druggists, but that at least an equal amount may be placed at the doors of medical men. Therefore, to stop up the loopholes with respect to wrongdoers who may be found among only one-fifth of all who are to have the right to supply the consumer, is to make a useless effort. It is reasonable to assume, that the improper traffic, which may now be carried on by some who constitute one-fifth of the total number, will be readily transferred, if necessary, to those who are now found among the other four-fifths to be guilty of such improper traffic.

Already I come to appreciate that my intended brief contribution is running away from me, and my further remarks will need to be confined to very brief statements. As a whole, the general intent and outline of the Harrison Bill, in view of constitutional limitations, should find approval. It means to accomplish the desired end by comparatively simple method. It places no particularly burdensome requirements upon either the manufacturing, wholesale or retail pharmacist. The method adopted for controlling and supervising all distribution among all dealers is likely to be effective. The rights of the legitimate retail pharmacist are not interfered with any more than is absolutely necessary, and no fair-minded pharmacist should complain with reference to the restrictions placed upon him, excepting in the matter of some important detail to which I mean to refer, but which it even now seems understood will be changed. But what is the use of giving expression to many things which are commendable, when primarily because of one practical defect the entire proposition is useless, and will produce no practical good. Even if everything else contained in the bill proves to be an exercise of the highest intelligence and as perfect as human mind can make, it is doomed to failure, so long as four-fifths of all who may lawfully supply the consumer, are not included within its most important provision.

Other defects to which I would point particularly are:

1st. That pharmacists who would fill a prescription for narcotics, are forced to know under penalty of fine and imprisonment, that the prescription is written by a physician who is also a registered dealer in narcotics.

2nd. The provision in Sub-section (b) of Section 2, which specifically limits the right to fill prescriptions to pharmacists. In my opinion such a provision in a Federal act is not constitutional. The exact same result is secured by substituting the word "dealer" for the word "pharmacist," and then because of legislation which exists in the

several states, only dealers who are pharmacists will be permitted to fill prescriptions.

3rd. Both Sub-Sections (a) and (b) of Section 2, in their present form, seriously endanger the constitutionality of the entire act, but this danger will be largely removed if the word "dealer" is substituted for the word "pharmacist," and if the exception and discrimination, with reference to record requirement as now made in favor of physicians, is removed.

All of these objections have been pointed out by the last Annual Convention of the N. A. R. D., and though the National Drug Trade Conference has been unwilling to admit or say, that it has acted on these objections, because so pointed out, the fact nevertheless remains that it has adopted changes which largely meet the objections, in all but the matter of requiring record keeping on the part of the physician when he assumes the functions of a pharmacist. Even in this respect, the Executive Committee of the National Drug Trade Conference has of late found itself compelled to advocate some record requirement, but in the form proposed it is wholly insufficient, because a dispensing physician could meet the requirement by entering in a book that he had dispensed one (1) ounce of cocaine on the fifth day of May, without stating to whom and in what quantity he had dispensed it to each of the separate parties. So far as I have been able to measure the needs with reference to record keeping by dispensing physicians, etc., it should be exactly the same as is now in the bill made applicable to pharmacists, and on the other hand, administration by the physician himself to the patient in cases of emergency should not require record keeping.

There are, of course, other provisions in the bill which deserve attention in its discussion, but I am sure that I have taken up enough time and feel also that others from whom you will hear are better prepared to discuss them. To be concise with reference to them all, I advocate such changes as are now advocated by the National Drug Trade Conference, excepting only its late proposition for record keeping on the part of the dispensing physician, which is insufficient to meet the needs of the case. I believe that every person, be he physician, dentist, veterinarian or pharmacist, who would supply the consumer with narcotics other than administration in cases of emergency, should be made to make, have and show the exact same kind of a record for every distribution of the drugs.

Very truly yours,

FRANK H. FREERICKS.

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## PERSONALITY.

Personality implies intelligence and self-consciousness. A beast is an individual, but not a person. The mere animal feeds itself, but is not conscious of itself. The seat of personality is the center of all our bodily and mental activities. The idea of the bodily structure does indeed enter into the general conception of the person, but it is related to it just as our clothes are related to our bodies—as a mere adventitious appendage. It is not essential to the reality of the person, as that which constitutes a man's self survives the body; it is not essential to the identity of the person, as that remains unchanged amid all the changes of the body. The personality of a human being is centered in that which thinks and reasons, and wills; which loves, and fears, and hopes; which suffers, enjoys and feels.—*George Bush.*

## Editorial Notes and Announcements

JAMES H. BEAL, Editor.....Scio, Ohio
ERNEST C. MARSHALL, Acting Editor,
63 Clinton Building, Columbus, Ohio

The Association does not accept responsibility for the opinions of contributors. Offensive personalities must be avoided.

Under the rules of the Postoffice the JOURNAL can be regularly mailed only to bona-fide paid subscribers. Subscriptions and association dues should be sent to the Treasurer, H. M. Whelpley, 2342 Albion Place, St. Louis, Mo.

All communications for insertion in the JOURNAL, or respecting advertising, requests for back numbers, and claims for missing numbers should be sent to the Acting Editor, 63 Clinton Building, Columbus, Ohio.

Claims for missing numbers will not be allowed if sufficient notice has not been given of change of address, and in no case if received later than sixty days from the date of issue

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### REPRINTS.

If the request is made at the time copy is submitted, authors will be furnished with not to exceed 50 reprints, without cover, of papers accepted for publication in the JOURNAL.

Larger numbers of reprints will be supplied by the Stoneman Press Co. at the following prices, provided the order is received before the type has been distributed:

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Orders for reprints may be sent either to the Editor, or to the Stoneman Press Co., Columbus, Ohio.

Under the heading, "The Pharmacist and the Law," will be found important amendments to the rules and regulations for the enforcement of the Food and Drugs Act. Under the amended rules the reception, by the Secretary of Agriculture, of guaranties from manufacturers and dealers, and the issuance of serial numbers, will hereafter be discontinued and all guaranties now filed will be stricken from the files and their serial numbers cancelled, and the use of such numbers is prohibited after May 1, 1915. The amendments further provide important regulations concerning the form of guaranty which may be given to dealers, in regard to their purchases and the manner by which it should be communicated, and relieves dealers from danger of prosecution when goods are purchased under such guaranty.

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The entire pharmaceutical profession of the country, as well as its members located in Ohio, are indebted to Prof. George B. Kauffman for his successful efforts to stay the unwise and extravagant attempts of ignorant officialism in Ohio, to annoy the members of the profession with absurd construction of the laws.

Without Prof. Kauffman's efforts in behalf of the sane construction of the insecticide laws, recently passed in Ohio, every druggist in the state would have been put to great annoyance and expense, but by his action in organizing the druggists to oppose the Agricultural Commission, a permanent injunction has been granted by the courts and a needed lesson has been given to officials everywhere, that a sane interpretation must be given to all laws, and that justice and common sense are the foundations upon which all laws should be based.

## A CORRECTION.

To the Editor:

Referring to the last paragraph on page 662, of the May issue of the JOURNAL, allow me to correct the statement therein, which implies that A. Schleimer introduced the use of cacao butter in making tablets.

As early as 1902 Edmund White (who now is President of the Pharmaceutical Society of Great Britain) and R. A. Robinson, Jr., contributed a paper which was read before the Dundee meeting of the British Pharmaceutical Conference, in which they proposed a mixture of one part of oil of theobroma and three parts of starch as a general excipient for tablets. At the Bristol Conference, in the following year, Edmund White and Henry Rodwell went further into the subject, and showed that by the use of an emulsion of theobroma the method could be used on a large as well as on a dispensing scale.

Yours very truly,

F. A. UPSHER SMITH.

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## THE AMERICAN DRUGGISTS' FIRE INSURANCE CO.

The regular quarterly meeting of the Executive Board of The A. D. F. I. Co. was held on May 15 and 16, all of the members of the Board being present.

The business for the first quarter of the year was shown to have made splendid progress, the insurance written during that time amounting to $3,834,934.70, at a net premium of $39,889.30, which shows an increase over the business of the first quarter of the preceding year amounting to $632,761.37, at a premium increase of $6,603.91.

Fire losses of the company for the first three months of 1914, amounted to $19,875.78, and the expense charged against the first quarter amounted to $11,162.40.

On the 31st day of March, the company had in force 7216 policies for insurance, amounting to $13,039,857.70, at a premium of $133,856.15. During the first three months of the year the company saved its policyholders $13,296.40 in their premium expense.

# College and Society

## MASSACHUSETTS COLLEGE OF PHARMACY.

The Forty-sixth Annual Commencement of the Massachusetts College of Pharmacy was held in Horticultural Hall, on Thursday, May 14 The Class Day program, at 2 p. m., was followed, at 3 o'clock, by the graduating exercises. The Class Day address of welcome was delivered by Charles Patrick Norton, the class history was read by Edward Louis Faucogney, and Joseph Hugh Cooney gave the oration. The prophecy came from Ralph Eliott Coburn. Alice Gardner Coleman made the Class Will, John Douglas Glancy, of the post-graduate section of the class, read an essay on Safe-guarding the Milk Supply, and the Farewell Address was delivered by Robert Edson Bemis.

President C. Herbert Packard presided at the graduating exercises. The prayer was made by the Rev. Frederick A. Wilmot, and the Hon. Samuel W. McCall delivered the Commencement address. Mr. McCall spoke of the importance of pharmacy as a profession and cautioned the graduates to have a care—in this age of specialization—that in their devotion to their work they do not allow themselves to become narrow, and he suggested that an active interest in the social, political and industrial problems of the day would, by fostering a broad open-mindedness, counteract the tendency to think and work along one line only.

The candidates for degrees were introduced to the President by Dean Theodore J. Bradley, who made a brief but thoughtful address to the class. As Mr. Lyman W. Griffin, the Secretary of the College, called the roll of the candidates for graduation, the President conferred the degrees, with some appropriate remarks to each individual student, afterward speaking to the class as a whole in his usual happy and forceful way.

Prize Nominations to Membership in the A. Ph. A. were awarded the following graduates

Joseph Hugh Cooney, for highest rank in senior organic chemistry; awarded by John G. Godding.

Emil Hermann Trumpold, for highest rank

in senior pharmacy; awarded by Prof. E. H. LaPierre.

Charles Patrick Norton, for highest rank in senior analytical chemistry; awarded by Prof. T. J. Bradley.

Robert Edson Bemis, for highest rank in senior materia medica.

Herman Jacob Epstein, for highest rank in senior general chemistry; both awarded by Pres. C. H. Packard.

The music for the afternoon was by the Salem Cadet Orchestra.

List of graduates, 32 for degree of Graduate in Pharmacy (including four women), and seven for the degree of Pharmaceutical Chemist:

Degree of Graduate in Pharmacy—Arthur Henry Barnes, Jr., Robert Edson Bemis, Elmer William Bennett, William Charles Bruzga, Herbert Francis Carbonneau, Ralph Eliott Coburn, Alice Gardner Coleman, Joseph Hugh Cooney, Joseph George Dion, Everett Leslie Emery, Herman Jacob Epstein, Edward Louis Faucogney, Edward Rudy Gifford, William Wallace Gifford, Nora Marceline Gobie, Kevork Gostan Gostanian, Charles Connor Hearn, Moses Jacobson, Bertram Francis Jones, Samuel Lourie, Emma Clare MacDonnell, Hortense Merrill, Howard Chamberlain Newton, Charles Patrick Norton, Frederick Vincent Palladino, Albert Solomon Pearlman, Samuel Kalil Saleeby, Earl Fuller Smith, Clarence Thompson, Eli Salmon Troupin, Emil Hermann Trumpold, John Francis Turner.

Degree of Pharmaceutical Chemist—Thos. Call Armstrong, Roy Chester Charron, Nicholas Ernest Dyer, John Douglas Glancy, Max Mackler, George Allen Moulton, Jr., Edward George Nagle.

The dinner of the Alumni Association complimentary to the class of 1914, at 6:30 p. m., was a very enjoyable part of the day, with about 130 people gathered about the tables. This dinner was at Horticultural Hall, as was also the class reception and ball, which was attended by many friends of the graduates.

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## ST. LOUIS COLLEGE OF PHARMACY.

The Twenty-ninth Annual Commencement exercises of the St. Louis College of Pharmacy were held on the evening of May 20th, at the Sheldon Memorial Auditorium, in St. Louis. The Hon. Charles Nagel delivered the valedictory address on behalf of the faculty.

The candidates for the degree of Graduate in Pharmacy and Bachelor of Pharmacy were introduced by the Dean, Professor H. M. Whelpley, and those for the degree of Pharmaceutical Chemist by Professor Charles E. Caspari. The following were awarded degrees:

Graduate in Pharmacy — Monte Earl Barnes, Lydia Frankie Batdorf, Frantz Frederick Berg, Edgar Van Bratton, Ph. B. '08, Louis Edward Brown, Coke B. Browning, Hillard D. Carlos, Jr., Thomas Bowden Chambers, George William Collins, Ph. B. '10, William Daniel Curran, Charles Raymond Davis, Clifford H. Fischer, Walter Freudenberg, Adam Guthrie, Jr., Ph. B. '12, Oliver O. Hedrick, Frank John Helms, Ernest Barthol Hoehn, John Atchison Hudson, Elmer Gaynor Joseph, Henry Adam Karber, Frank Kincaid, Louis Oscar Kloeckner, William Krummenacher, Charles Lasersohn, Junius Blanton Linn, Willard McKee Lyons, William Paul Massock, Albert Henry Mayerhoffer, William Leslie McQueary, Fred George Messerschmidt, Edwin Archer Monell, Albert Willian Mueller, Arthur August Overman, Cressie Delahae Panhorst, Cecil Robert Parks, Alexander Pearlstone, Virgil Earl Pirtle, Benjamin James Pope, David S. Ralston, Ph. B. '12, Walter Augustus Reese, Ph. B. '12, Edwin Jerome Rhein, Kenneth Parke Riley, Edwin Louis Schroeder, Verner Franklin Smith, Gilbert Spieldoch, Mrs. John Esther S'Renco, Hans Alwin Weber, Odus Pharr Wilkinson, Lee Howard Witty, Claud Oakley Wright.

Bachelor of Pharmacy—William Francis Brennan, Hull Wesley Butler, William Henry Duckworth, Arthur Henry William Charles Kloepper, Charles F. Lanwermeyer, Chester William Lieder, Albert Leo Spaedy.

Pharmaceutical Chemist—David S. Ralston.

The awards for honors were as follows:

*Senior Class Scholarships and Prizes.*

The Alumni Prize, a gold medal, conferred upon a candidate for the degree of Graduate in Pharmacy for the best examination in all branches, is won by Frantz Frederick Berg.

The College Silver Medal conferred upon a candidate for the degree of Graduate in

Pharmacy for high averages in all branches, is won by Frank John Helms.

The recommendation for membership in the American Pharmaceutical Association, with dues for 1914 given by the college, is awarded to Junius Blanton Linn.

Honorable mention: Graduate in Pharmacy Class—Miss Cressie Delahae Panhorst, Miss Lydia Frankie Batdorf, Fred George Messerschmidt, Alexander Pearlstone, Walter Freudenberg, William Paul Massock.

Honorable mention: Bachelor of Pharmacy Class—William Henry Duckworth.

*Junior Class Scholarships and Prizes.*

The Edward Mallinckrodt Scholarship for 1914-15, Joseph Frey.

The Meyer Brothers Scholarship for 1914-15, Glenn Adrian Burkhart.

The J. S. Merrell Scholarship for 1914-15, Roland Henry Kraege.

The Alumni Prize, some Standard Work on the subject of Pharmacy, or allied branches, Herbert W. Bixon.

Honorable mention: Junior class—Joseph Frank Evans, Sam Honigberg, Philip Ludger Chiles.

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## KANSAS CITY COLLEGE OF PHARMACY.

The Twenty-ninth Annual Commencement of this institution was held on Thursday evening, May 7th, at Spalding's Auditorium. The members of the graduating class were: Charles A. Bailey, Paul H. Blinn, Ralph E. Foster, Anna Freesman, James J. Flynn, Roscoe M. Hutchinson, Cristobal Martinez, W. Frank Malson, Clyde W. Moll, W. R. McDanel, Walter F. Probst, Ray O. Piper, George A. Walkup, Sumner R. Williams, Harry E. Price, Earl Dewees, George E. Seidler.

The Junior Medal was awarded to Giles E. Wickmire, of Larned, Kansas, and honorable mention was given to Harry Kelly and Thos. D. Evilsizes, of Kansas City.

The Alumni Medal for Chemistry was awarded to Ralph E. Foster, of Perry, Oklahoma, who also received the College Medal for highest general average in all courses. James J. Flynn and Roscoe M. Hutchinson received honorable mention.

The annual ball given by the Alumni Association to the graduating class occurred on the evening of May 5th, at Drexel Hall.

Mr. and Mrs. D. Victory Whitney were members of the Reception Committee. Professor Whitney is Director of Pharmaceutical Laboratories and Professor of Pharmacy, and Mrs. Whitney is Professor of Botany and Pharmacognosy at the College.

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## NEW JERSEY PH. A.

The New Jersey State Association will hold its annual meeting on the 16th, 17th, 18th and 19th instant, at the New Hotel Breslin, Lake Hopatcong, and a most pleasurable and profitable meeting will undoubtedly result from the very comprehensive scope of the program outlined. This association is one of those which seems to have successfully solved the question of combining properly the entertainment features with those involving solid instruction, profitable to every member. The list of queries proposed as subjects for papers should be most fruitful of results in the way of information of weighty import, not alone to the members of this association, but also to the pharmaceutical profession at large.

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The Pennsylvania Pharmaceutical Association will hold its annual meeting at Buena Vista Spring Hotel on June 23-24-25. From the very interesting list of subjects for queries, sent to the members, some papers of exceeding interest to the trade are to be looked for.

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The Massachusetts State Pharmaceutical Association will convene at the New Ocean House, Swampscott, for the thirty-third annual meeting on June 16-17-18. The program promises a very interesting and pleasurable meeting.

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## WOMEN'S PHAR. ASSOCIATION PACIFIC COAST.

The regular monthly meeting was held April 24, 1914, in the Assembly Hall, San Francisco. Mrs. R. E. White, the President, presided.

The roll call showed a large attendance. Discussions were held on Isotonic Salt Solutions, the preparation of Extract of Malt and Cod-Liver Oil, Methods of preparing Ichthyol Capsules, Iodothyrine and Thyroidectin.

A communication was received from Miss Clarissa Roehr, Secretary *pro tempore* of the San Francisco Branch of the A. Ph. A., inviting the participation of the members in the next meeting of that Branch.

Miss Mabel Dolcini read a paper on Ozone, and Mrs. F. F. Rajotte presented a paper on Boils. The discussion of the evening was on The Card-Index for Stock, and Miss Nelson,

Mrs. White, Miss Dolcini and Dr. Winslow spoke upon that question.

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## ATLANTA WOMAN PHARMACIST CLUB.

The Atlanta Woman Pharmacist Club met in the library of the Southern College of Pharmacy, April 24th, 1914, for the purpose of forming a permanent organization.

Dr. R. C. Hood, Dean of the Southern College of Pharmacy, acted as temporary chairman.

The following list of officers were elected: Miss Margaret Kimmel, President; Mrs. G. E. Matthews, Secretary, and Miss Bertha Davis, Treasurer.

It was voted that the club retain the title "Atlanta Woman Pharmacist Club."

The purposes of the club are to keep its members informed of the advance of the pharmaceutical profession, to uplift woman's position in the pharmaceutical world, and to meet socially for the entertainment of its members and guests.

Miss Bowie read an interesting paper entitled "Woman in Pharmacy," and it was decided that at each meeting the members would read papers, tell of the interesting things met with in their work, and make suggestions for the good of the club and its members.

The matter of fees being brought before the meeting, it was voted that each member be assessed an initiation fee of 25 cents and regular dues of 20 cents per month.

It was also voted that the regular meeting of the club be held on the third Friday of each month.

After the business meeting, refreshments were served.

The meeting then adjourned to meet Friday, May 15th, 1914.

MRS. G. E. MATTHEWS, Secretary.

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## KANSAS PHARMACEUTICAL ASSOCIATION.

The Kansas Pharmaceutical Association met at Hutchinson on May 12, 13 and 14. There was a very gratifying attendance of the members, notwithstanding that the meeting-place was far from all the large cities and in the less-densely populated western portion of the state.

The address of President C. C. Reed was replete with timely suggestions of benefit to the members of the profession. Secretary D. v. Reisen reported a large amount of work accomplished in many ways for the relief of vexatious conditions affecting the trade, and an increase of membership in the Association,—seventy-nine members being added during the past year, making a total roll of nearly six hundred and fifty.

The Association voted to continue its affiliation with the N. A. R. D. and also that, in the future, members of the Kansas State Board of Pharmacy shall not be eligible to serve more than two successive terms.

The special guest of the occasion was Mr. Thomas H. Potts, the National Secretary of the N. A. R. D. To the great regret of all present Mr. Potts was unable to take part in all the proceedings of the meeting, owing to a sudden illness, from which he did not entirely recover until after the adjournment of the meeting.

Dr. J. B. Wood, representative of P. D. and Co., read a very interesting paper on "Biological Products," which was of much interest to the members, and Mr. R. E. Bell, of Frederick Stearns & Co., contributed a paper upon "Cooperation," from which many of the members derived a number of ideas which will undoubtedly result in profit to them.

A special commemorative meeting was held by the Association in memory of Mr. Charles M. Becker, late of Ottawa. Mr. Becker served for many years as a member of the Kansas Board of Pharmacy. Many of the members paid a fitting tribute to his name and memory.

The following board of officers was elected: President, Walter J. Bangs; First V. P., J. W. Giesburg; Second V. P., E. E. Bloom; Secretary, D. v. Riesen; Treasurer; John Schmitter.

The Association were the guests of the Traveling Men's Association at a banquet given at the Bissante Hotel. Plates were laid for three hundred guests and the affair reflected much credit on the hosts.

The ladies were charmingly entertained during the days of the convention by a musicale and women's reception and a grand ball at the Elks' Club, and every minute of their stay in Hutchinson was made enjoyable.

Mrs. C. E. Wherrett was elected President, and Mrs. N. C. Edelblute, Secretary of the Ladies' Auxiliary.

It was voted to hold the next meeting at Wichita, May 11-12-13, 1915.

# Proceedings of the Local Branches

"All papers presented to the Association and its branches shall become the property of the Association, with the understanding that they are not to be published in any other publication than those of the Association, except by consent of the Committee on Publication."—By-Laws, Chapter X, Art. III.

Reports of the meetings of the Local Branches should be mailed to the Acting Editor on the day following the meeting, if possible. Minutes should be *plainly* written, or typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly, and manuscript should be signed by the reporter.

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## CHICAGO.

The Chicago Branch of the A. Ph. A. was honored at its April meeting, the evening of the twenty-first, with an address by Professor John Uri Lloyd of Cincinnati. Professor Lloyd's subject, "The Evolution of American Materia Medica," led to many reminiscences and his talk was very earnestly received by the audience.

Secretary Gathercoal introduced the new A. Ph. A. button, samples of which had been received from Treasurer Whelpley and orders were taken for twenty of the buttons. They were voted very neat in design and excellent in finish.

The May meeting will be devoted to a criticism favorable and unfavorable of the changes in the monographs of galenicals for the new pharmacopœia as recently published by the Revision Committee. Several pharmacists, members of the Branch, led by I. A. Becker, pharmacist at Michael Reese Hospital, are preparing criticisms to be presented at this meeting.

E. N. GATHERCOAL, Secretary.

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## CITY OF WASHINGTON.

The April meeting was held on the sixteenth of that month at the National College of Pharmacy.

The director of the National Vaccine and Antitoxin Institute of Washington, D. C., Dr. J. R. Stewart, described to the large number of members and guests, and to the entire senior class of the National College of Pharmacy, present by special invitation, in a most interesting and detailed fashion, the origin and development, manufacture, characteristics, and peculiarities of each vaccine and antitoxin now in practical use, and outlined the character of experimental work now being conducted to increase the scope and efficacy of this form of medication. He supplemented his address with exhibits showing antitoxins in various stages of manufacture and with demonstrations of the uses of various types of syringes.[1] Following his address, he answered all questions propounded to him concerning this line.

When he took his seat, he was given a rousing vote of thanks.

The May meeting was postponed to June 6, 1914, when the branch will visit the Department of Agriculture Drug Farms, opposite the Arlington National Cemetery, in Virginia, at 1:30 p. m. At this meeting, Dr. Stotsenberg, who is in charge of the farms, will, after showing the members around, give a talk on drug plant culture, fake money-making schemes involving such culture, and a number of other subjects interesting to the retail druggist and to the general public.

HENRY B. FLOYD, Secretary.

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## DENVER.

At the meeting in March, Mr. A. W. Clark read the following paper on "Trade Conditions."

Mr. Clark prefaced the delivery of his paper by reading a clipping from a trade journal which strongly advised that a proprietor should "stand-in" with his clerks. The clipping stated that it was quite as commendable an aspiration to desire to "stand-in" with clerks, as it was to wish to "stand-in" with the public, and that a man who only hires clerks to do the small things in his business will always have a small business.

Mr. Clark, continuing, said:

I shall not attempt in this paper to make an elaborate analysis of trade conditions, or to give the reasons for them, for, as the viewpoint of every business man is obtained, as a rule, from the front-door of his own store, every one has reasons of his own for their existence, and his remedy for those

[1] Dr. Stewart's paper appears in another portion of this issue.

conditions which need reformation. My only purpose in reading this paper is to attempt to entertain you; to assist you in passing a pleasant hour in a social way, and to offer to you, only in a general way, a few suggestions for your consideration. Our Branch meetings have been a source of pleasure to me and I presume every member should do his part toward making them of enjoyment and profit to all the members, and it is with that purpose and desire that I offer these suggestions for your consideration.

It seems to be generally conceded that trade is not what it should be and does not amount in volume or show sufficient profit to justify our present expensive methods of securing it.

How may we better these conditions?

Reducing the expense account naturally comes up for consideration first, but this does not always bring the desired result, especially if it is done at the expense of the quality of service furnished.

To cover the field of local drugdom and furnish actual statistics would take much time, besides I am at a loss to know just where to go for the information and facts that will show the real conditions.

The jobber and the banker might furnish some very interesting material, but to make matter of this nature public would be a rank violation of business ethics.

I here suggest as a general underlying principle to be adopted by the man of limited financial resources when starting in business, that he consult and advise frequently with his jobber and banker, making correct statements to them regarding his resources and as his business may progress, of his sales-credits, etc., and that he consult with them both before contracting any considerable debt or signing of binding contracts, etc.

By doing this he will have time to consider the thing himself that he proposes to do, and he will have the advice of the man that has, as a rule, a much broader business experience than he himself possesses.

I believe that many business men would gain very materially by adopting this rule, men that may have been in business for years as well as the young man just nosing his way in.

It is not necessary to suggest this policy to experienced men for it is presumed that they know the importance of it and have benefited by it.

It seems to be the opinion of some that the business of an attorney is to get their clients out of trouble, but as a matter of fact the real business of an attorney is to keep them from getting in, therefore it is well to be advised before acting, and to whom may we go for that advice more freely than to the ones that prosper as we prosper, or who suffer loss should we fail, viz.: the jobber and the banker.

If the above suggestion had been adopted by all our local business men, conditions in Denver, I venture to assert, might be far better than they are today.

As we look over the local field, seemingly, we find too many persons trying to operate or to conduct drug stores.

This statement seems to be substantiated fully if we may judge their success by their financial rating.

Had some of these advised with their jobber or banker I do not believe they would have gone into business.

This condition of an excess number of stores seems to be found more frequently in the city than in the country.

"Can we find any remedy for it that is practical?" is a question often asked.

The elimination of the less competent and the survival of the stronger and better qualified is the usual rule that maintains, and this will in time undoubtedly apply here—it is gradually working out that way. It may be possible to hasten this elimination process by consolidating several stores in one, to be operated under the combined management of the several now independent proprietors.

For instance, when by close application and long hours several stores are operating and each supporting in a limited way, one person, would it not be possible to consolidate several of these stores, giving one three-man store in place of three stores of one man each, and giving better working hours, a fair remuneration and better opportunity to enjoy some of the blessings of our God-given sunshine and the glorious mountain scenery that lie at our very doors,—scenery and sunshine and pure air, not excelled in any part of the known world, all this, without price and with but very little effort, may be enjoyed in Colorado.

Then again, another remedy might be for the proprietor to just simply forget that his store is called a drug store, just forget the drug end of the term and operate a good

store, a little neighborhood store, with a notice on the door, "Open at 8 a. m., close at 6 p. m.; no Sunday business."

Considering the curtailing of expense and satisfaction that would be derived, our proprietor might find himself as well-off financially at the end of the year, as he does now working under present conditions.

This is not intended to reflect on the small man simply because he is operating a small store, but is offered just as a suggestion to fill in, and in all seriousness, the fact remains, that it is almost impossible to do any considerable amount of prescription work in any considerable number of stores in Denver, for the reason prescriptions are not written in proportionate number to the number of drug stores. The wide range in the number of articles possible for the physician to prescribe, and the great number of physicians writing prescriptions in a city the size of Denver make it impossible for the majority of stores to stock all of the items prescribed, that are more or less in daily demand.

To put it another way, comparatively, there are only a few druggists that are justified (considering the limited demand) in stocking all the remedies that are in general use.

The consolidation of several stores in each district, would remedy the conditions just stated and if this be done in all parts of the city, more complete stocks might be carried at a profit where now they show a loss. The people would be better served and a waste, that is now almost criminal from an economic viewpoint, would be corrected and saved.

Will this condition ever be remedied by the American people? For this condition, being true of Denver, applies to other cities in this country.

Making a low price on drugs does not bring more business. Generally speaking, people do not buy more drugs because the drugs are cheap or sold at a low price, that is, in the same way one might buy clothing or merchandise. A man might buy two shirts instead of one, if the price be attractive, but we do not presume he would take two doses of castor oil simply because he could get the two for the price of one.

As a rule the doctor that gives his services for a dollar, does not have as many patients as the two or five-dollar man. After all, it is not so much the price in either case as it is the man.

If the price of drugs be reduced one-half in the city of Denver, we do not presume( barring the joy-producing variety) the amount consumed would be very materially increased. The personality of the man is reflected in his establishment, be it large or small, and is a special factor in making for success or failure. This applies to all mercantile houses, it extends to railroad management and very much so in the operating of a drug store or pharmacy.

To our methods of doing business we might apply the old saying: "It is not what you do but how you do it."

Then again, it is well to watch the successful man, the man that succeeds. Contact with better men, generally is of benefit to the man that may not be quite so good. We all have much to learn in this game called "trade."

There is an evolution going on in drugdom, in Denver, and in the nation, and no man can stay it or turn the tide very materially. We, as individuals, may assist in the moulding or shaping of it, but we cannot expect to have everything our way.

Large financial interests are taking over numbers of drug stores in the thickly populated centers, seemingly for the purpose of securing an outlet for certain lines of goods.

It does not seem to be their purpose to elevate pharmacy, or the pharmacist, in the way many have hoped for, but, seemingly, their purpose is to commercialize pharmacy, and incidentally the pharmacist.

These conditions, fortunately, have not been as pronounced in Denver as in some other cities.

We seem to have entirely different local conditions to contend with—different from Eastern and different from Western in many respects.

If Denver were a larger city, we might expect them to prevail here.

In the years that have passed, we, in Denver, have prospered to a greater degree than some of our less fortunate brethren in the East. We have have had coöperation of the jobber and the retailer, something that has not existed in many Eastern cities, of any considerable size.

Just what the future has in store for us, no

man knows, but let us remember the principles which have stood for prosperity. Do not turn from the old to the new, without considering what is to be gained by the turning.

It seems that much might be gained by legislation and enforcement of present laws —laws that are supposed to protect the people and benefit us as well.

If our laws are unjust and do not correct the evils that exist, let us try and amend the same.

Our Board of Pharmacy should be of service to us in regulating the pharmacy end of our business. Let us work with them to bring about this result. Surely the raising of requirements for qualification, with enforcement of the law, will eventually help to some extent, and at the same time guarantee to the people better and more intelligent drug store service.

Our State Board of Health should work advantageously with us in correcting many evils, that some think now exist.

Every druggist should be willing to assist them in enforcing the law.

The act of March 3, 1907, regulating the sale of food and drugs in Colorado, is in the main good, and, having a standard for drugs, we have an advantage over the grocery man, who really has no standard for many food products.

As business men, we should not feel that we must depend upon the law to protect us, over and above any other class of citizens. We should first learn to protect ourselves. Being amenable to the law and contributing to its support, we have the right to expect the benefit that may be derived from an intelligent enforcement of it.

If our fellow druggists could but realize the benefit gained by social contact in our Branch meetings—even in the way of trade betterment—we would soon have to secure a larger meeting room.

While a talk of this nature may touch upon only a few of the many viewpoints of trade, it may sandwich in with some of the more scientific and interesting ones, for pharmacy and merchandising seem to go hand in hand, more and more, and the pharmacy of the future may be more commercialized than it is today, if the signs of the times are correctly interpreted.

## SAINT LOUIS.

The Saint Louis Branch met in regular session at the College of Pharmacy on Friday evening, April 17th, with President Wilkerson presiding. The minutes of the previous meeting were approved as read.

The Chair then briefly outlined the talk he gave before the Saint Louis Pharmaceutical Society, with the view of uniting that Association with the A. Ph. A. Branch. After some discussion, a motion was made and carried, that a committee be appointed to confer with a committee of the Society to ascertain the feasibility of uniting the two associations. The Chair appointed on that committee, Messrs. Mackelden, Buehler and Bierman.

The subject for discussion was, "Shorter Names and Synonyms for some U. S. P. and N. F. Preparations." Mr. E. A. Sennewald cited a list of U. S. P. preparations which in his opinion should have shorter names or synonyms. Professor Good read a list of synonyms and shorter names that have been presented to the revision committee for some U. S. P. preparations.

The following motion received unanimous indorsement:

*Resolved*, "That the use of coined names in the United States Pharmacopœia, should be discouraged except those applied to well known products which are no longer protected by patent or proprietary rights."

It was further moved and carried that a copy of this motion be sent to Professor Joseph P. Remington, Chairman of the Revision Committee.

Mr. Mackelden brought up the subject of summer meetings, stating that these outings help to keep up interest in the Branch. A motion was adopted that the President appoint a committee to arrange for summer outings, and Messrs. Mackelden, Hoester and Kring were appointed as that commitee.

JULIUS C. HOESTER, Secretary.

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## PITTSBURGH.

At the May meeting much valuable instruction was given concerning the use of collapsible tubes for the dispensing of ointments, by Dr. F. J. Blumenschein. In opening the subject, the doctor said, "The trend of the times is toward cleanliness, and this trend should find the pharmacist leading the procession. One of the ways by which he can keep to the front is in the use of clean and progressive methods in compounding and dis-

pensing. While most of the pharmaceuticals are being standardized, and methods for improvement in manufacturing and marketing are being proposed, the ointments and allied products are being neglected. Ointments are dispensed in all kinds of containers,—bottles, tin and wood boxes, porcelain and glass jars of various colors,—without a thought as to whether the preparation is affected by light, air, moisture or the container itself. Collapsible tubes for prescription work should be made of pure (block) tin. This should be insisted upon, as they are often made of alloys of lead and other injurious metals. The advantages of collapsible tubes are many. First, the patient can use the last portion of the ointment, with the knowledge that it is just as free from contamination as the first portion, and, second, the dispenser is not required to handle a returned container, from which he might contract anything from simple itch to smallpox. A canvass of the oculists, to learn why they so frequently prescribe ready prepared ointments in tubes, revealed the fact that, while they prefer freshly prepared ointments, they are willing to prescribe something which, while not as good, yet always carries the assurance of being clean. Of course, all ointments cannot, owing to their composition, be dispensed in metal tubes, yet a great many may be so dispensed. The cost is but slightly greater, and they require a little more time to prepare, but these disadvantages are greatly offset by the fact that a better price can be demanded and increased prestige gained by doing things right.

"Ointments which have been fused, or that have to be sterilized, can be readily poured into the tube; others can be placed in waxed paper and rolled into a cylinder in the hand, then placed in the tube and by partly closing the paper, it can be drawn out, leaving the ointment in the tube."

The subject of "The Sale of Heroin; Its Legal and Moral Status," was discussed from every viewpoint, by Drs. J. A. Koch, G. W. Kutscher, Louis Emanuel, President Andrew Campbell and B. E. Pritchard. A motion was unanimously adopted, commending the Harrison Anti-Narcotic Bill now pending in the Senate, and instructing the Secretary to convey to Senators Penrose and Oliver the request of the Pittsburgh Branch, that they urge the immediate passage of the measure in the interests of humanity.

B. E. PRITCHARD, Secretary.

## NASHVILLE.

The Nashville Branch of the A. Ph. A. held one of the most interesting meetings of the year, at Furman Hall, Vanderbilt University, May 14, with Dr. J. O. Burge in the chair.

Dr. J. M. Rogoff made a preliminary report of some pharmacological experiments he has been making, to determine the amount of deterioration of aqueous alkaloidal solutions. His work, so far, has been confined to that upon solutions of morphine, atropine, pilocarpine and strychnine, testing them upon cats and frogs, and his results indicate a gradual deterioration of these solutions with age. His final results will be reported to the Scientific Section of the A. Ph. A., at the Detroit meeting. A paper entitled "Board of Pharmacy Questions," was read by W. R. White, and discussed by Messrs. Ira B. Clark, M. E. Hutton, Dr. E. A. Ruddiman and Dr. J. M. Rogoff. The subject for the evening, "Shorter Hours," was then taken up for discussion.

The Secretary read the results obtained, by sending out 200 return cards. These showed that 84 percent favored shorter hours, and that 92 percent favored closing certain hours on Sunday, but there was much divergence of opinion as to the best way of accomplishing the reform. After remarks by various members, the Branch adjourned until September.

W. R. WHITE, Secretary.

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## PHILADELPHIA.

The regular monthly meeting was held at the Drug Club, on Tuesday evening, May 5. After hearing the reports of the officers and of the various committees, it was decided, upon motion by Mr. W. L. Cliffe, to recommend to the American Pharmaceutical Association that the proposed national headquarters be located in Philadelphia, and the committee was directed to communicate with the proper officials of the parent body, and advise them of the advantages which Philadelphia possesses for the proposed headquarters.

A vote of thanks to the Philadelphia Drug Club for the use of its rooms for meeting purposes during the past year, was proposed and unanimously carried.

The program of the evening consisted of a discussion of the Harrison Bill and other legislative questions of state importance. Professor Charles H. LaWall presented a

paper entitled "Some Pennsylvania State Laws, Other than Pharmacy Laws, Which affect the Retail Druggist."

Secretary R. P. Fischelis presented a brief review of the Harrison Bill and amendments, and read communications from Messrs. Samuel L. Hilton, Martin I. Wilbert, A. Hopkins Stewart and F. H. Freericks, on the same subject.

C. Mahlon Kline spoke at length on the proposed anti-narcotic legislation, telling of the work of the National Drug Trade Conference and of the various state laws which propose to regulate the traffic in narcotic drugs. Mr. Samuel C. Henry gave the views of the N. A. R. D. on this question, and also spoke favorably on the Nelson Amendment now before the Senate.

At the conclusion of the discussion, it was voted that the Philadelphia Branch go on record as approving the purpose of the Harrison Bill, and as favoring the Nelson Amendment. This being the last meeting before the summer recess, adjournment was taken until October.

ROBERT P. FISCHELIS, Secretary.

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## NEW YORK.

The April meeting of the New York Branch of the American Pharmaceutical Association was held at the College of Pharmacy on the 13th, with Professor Arny in the chair, and with Louis Berger acting as Secretary, in the absence of Secretary McCartney.

Treasurer Weinstein reported a balance of $98.87 in the treasury. Chairman Anderson, of the Legislative Committee, informed the Branch regarding conditions at Albany, reporting the passage of the Walters-Seelye Bill placing the regulation of the hours of labor for drug clerks back under the pharmacy act, and of the Boylan anti-narcotic bill. Dr. Anderson also spoke of the amendment proposed to the Harrison Bill, relative to keeping a record, by physicians, of narcotics dispensed by them, and of the opposition created thereby. The progress of the Stevens price-maintenance bill was reported, as well as an announcement of the approaching meeting in interest of the bill.

Dr. George C. Diekman, Chairman of the Committee on the Progress of Pharmacy, read an interesting report, which discussed for the most part the work of the German Apothecaries Society, notably at the Universities of Berlin and Goettingen, on the examination and exposure of questionable proprietary medicines. The following items were dealt with:

Salicol—a tablet marketed by Dr. M. Weitemeyer, of Erfurt, said to contain aceto-salicylic and citro-salicylic acids, which upon investigation of Von C. Mannich and L. Schwedes, was found to consist of aceto-salicylic acid. The claim made that the tablet contained in addition to the above, citro-salicylic acid, was pointed out to be false and misleading.

C. Mannich and G. Leemhuis, in Apotheker Zeitung, No. 19, 1914, page 194, report on the examination of codeine tablets, as follows:

The investigation was undertaken in response to the request of the German Apothecaries Society. The tablets were claimed to contain 0.05 gm. of codeine phosphate each, and had been obtained by a physician through agency of a mail-order concern. Upon examination the tablets were found to be uneven in size and thickness. This variation was very material.

In weight these tablets varied between 0.16 and 0.25 gm. For purpose of ascertaining the codeine content, the following procedure was employed. Ten tablets, weighing 2.07 gm., were treated with 10 gm. of diluted solution of sodium hydroxide, until they disintegrated. The mixture was then shaken out with 100 cc. of ether. Forty cc. of the ether containing the basic codeine were allowed to vaporize at low temperature, and the residue (codeine) dried at 100° C. and weighed.

The residue thus obtained was found to weigh 0.1829 gm. for the 10 tablets, which equals 0.01829 gm. for each tablet. As a control, a determination of the phosphoric acid, by the ammonium molydbate method, was carried out. The amount of phosphoric acid found corresponded closely to the amount of codeine found. Calculation shows that each tablet contained 0.015 gm. of codeine phosphate, instead of 0.05 as claimed.

It would therefore seem that the quantity of codeine phosphate was mis-stated, and that each tablet contained only about one-third of the quantity claimed.

M. Pawlewskis' Eye-Water, which was claimed to strengthen weak eyes, cure cataract and glaucoma, heal inflamed eyelids, granulated eyelids, cure scurvy and bleeding of the gums, was found to contain zinc sul-

phate 1.25 percent; sodium chloride 1.32 percent; water q. s., and it was pointed out that extravagant claims had been made for an old and well-known preparation which is being marketed under a new name.

Schumacher's Cell Regenerator, No. 13, was reported in Apotheker Zeitung, No. 18, 1914, page 186, by C. Mannich and S. Kroll, as consisting entirely of sugar of milk.

A physiological determination of the value of certain digitalis preparations was made by Von Dr. Anton Lehnert, Bad Duerkheim; and Professor Oswald Loeb, Goettingen:

The authors examined a number of well-known digitalis preparations, with a view to establishing their therapeutic value in a physiological way. They employed the method of Frankel-Gottlieb, comparing the results found, in the examination of the preparations, with the results found upon using an infusion of digitalis, prepared from titrated digitalis leaves obtained from the firm of Caesar & Loretz.

The folia digitalis titrata, of Caesar & Loretz, was found to show a constant therapeutic value when tested from year to year, which the authors state to be as follows: Each 0.1 gm. of the substance is the equivalent of 5 Gottlieb units.

A Gottlieb unit is designated, the smallest quantity of substance required to produce a systolic cessation of heart-action in a frog, weighing from 29-32 grams, with certainty, within 30 minutes.

Digitalis dialysata Golaz: The preparations intended for intravenous injection, showed only from 16 to 40 percent of their claimed value. The preparations intended for internal medication were found to correspond in their declared value.

Digifolin: This preparation is placed on the market, both in solution and tablet form Its activity conformed closely to the claimed values, and the contents of the packages were found unchanged after 11 months.

The authors claim that their results have been confirmed by other investigators.

An exhaustive report on concentrated ipecac infusions was referred to as having appeared in Phar. Zentralhalle, 1914, No. 11, page 249, the authors of which were Von C. Mannich and W. Duehr, and the conclusions reached were as follows:

(1) That a properly prepared infusion of ipecac contains only about three-fourths of the alkaloidal value of the drug employed.

(2) That an infusion prepared with the aid of a concentrated infusion (1:20) formula of Dieterich, contains only two-thirds the quantity of alkaloid, as will be found in a properly and freshly prepared infusion.

(3) That alkalies should under no circumstances be added. This is sometimes done in order to impart a deeper color to the product.

(4) That the concentrated preparations of the market are unreliable, and that they always contain a much lesser quantity of alkaloid than an infusion properly made.

The report was discussed by Messrs. Raubenheimer, Latham and Weinstein.

Dr. Diner called attention to the approaching meeting of the State Medical Society, to be held at the Hotel Astor, and moved that the Branch send delegates. The motion was carried.

Dr. J. L. Mayer then read the paper of the evening, entitled "The Standardization of Volumetric Acid and Alkali Solutions."*

The paper brought out an interesting discussion, participated in by Messrs. Schmidt, Roemer, Raubenheimer, Niece and Arny.

LOUIS BERGER, Acting Sec'y.

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## SAN FRANCISCO.

Thursday evening, May 12th, the San Francisco Branch of the American Pharmaceutical Association was permanently organized. The following officers were elected: President, Dr. Albert Schneider; First Vice-President, Jennie M. White; Second Vice-President, Arthur Reum; Secretary-Treasurer, Clarissa M. Roehr; Council Member, Dr. A. Schneider.

Communications were received from Mr. J. W. England and Dr. F. E. Stewart. Mr. England, as Secretary of the Council, conveyed the unanimous approval of that body to the organization of the San Francisco Branch. Dr. Stewart congratulated the members and wished the future success of the Branch.

The following program was presented during the evening:

The United States Pharmacopœia:—

"From the Standpoint of the Chemist," by Arthur Reum.

"From the Standpoint of the Pharmacist," by Clarissa M. Roehr.

*This paper appeared in full in the last issue of the JOURNAL.

"From the Standpoint of the Pharmacognosist," by Dr. A. Schneider.

"The Italian Pharmacopœia," by Dr. A. S. Musante.

"The British Pharmacopœia," by Miss M. Low and Mrs. R. E. White.

"The Homeopathic Pharmacopœia," by Mr. Lengfeld.

Discussions on the German Pharmacopœia and on the French Codex were postponed to a later date.

The next meeting will be held on June 9th in the office of the Pacific Pharmacist. The members will discuss a paper on "Some Points for the Pharmacist Regarding the Products Used in Organo-therapy," by Dr. John Zieg.

CLARISSA M. ROEHR, Secretary.

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## CINCINNATI.

The first annual meeting of the Cincinnati Branch, A. Ph. A., was held at Lloyd's Library, May 12, with Vice-President Prof. Theo. D. Wetterstroem in the chair.

The Treasurer, Mr. F. S. Kobbe, presented his annual report, which was accepted, and a vote of thanks was tendered him for his efficient service.

The Secretary followed with a complete record, covering the work of the first year's life of the Branch. The report was accepted with a recommendation to preserve the original minute book and its insertions.

Mr. Edward Voss, Jr., Chairman of the Committee on Membership, reported for that committee.

Prof. C. T. P. Fennel, Chairman of the Committee on Pharmaceutical Progress, made a report and, being the accredited member of this Branch to the Council of the parent body, he gave information regarding the work accomplished by the Council. A resolution of regret regarding the resignation of Prof. J. H. Beal as General Secretary, was passed, deploring the necessity for the retirement of one who has performed such efficient service in the cause of American Pharmacy.

The annual report of the Legislative Committee was presented by Hon. Frank H. Freericks in a very comprehensive manner, covering the different pending bills of state and national importance, such as the Duffy Anti-Narcotic Bill, the Itinerant Venders' Bill, the Stevens Bill, the Harrison Bill, the Clapp Bill and others. The report was accepted, and it was voted that it be sent in its entirety to the JOURNAL for publication.

The presiding officer, Prof. Theo. D. Wetterstroem, read the following resolution, passed by the Agricultural Commission of Ohio, April 28, 1914:

"The Agricultural Commission of Ohio interprets the Insecticide and Fungicide Act and the Feed Stuff Act as exempting from their provisions all drugs, chemicals, etc., recognized by the U. S. P., N. F. or other recognized standards; all preparations extemporaneously prepared or compounded for customers for consumption and not for resale; all preparations for which no claims are made for insectidal or fungicidal properties, and all proprietary medicinal preparations and stock foods upon which license-fees have been paid by the manufacturers."

It was decided to incorporate this resolution in the report of the Legislative Committee.

Mr. Chas. G. Merrell made a report for the Committee on Transportation to the A. Ph. A. meeting, and was followed by the Chairman of the Nomination Committee, Mr. Edw. Voss, Jr., who presented the following ticket:

President, E. H. Thiesing; First Vice-President, F. W. Weissmann; Second Vice-President, J. F. Kutchbauch; Treasurer, Julius Greyer; Secretary, Chas. A. Apmeyer; Executive Committee, A. O. Zwick, three years; C. T. P. Fennell, two years; C. G. Merrell, one year.

The report was signed by F. S. Kobbe, Wm. L. B. Brittain and Edw. Voss, Jr., Chairman.

The report being duly accepted, the Secretary was instructed to cast one ballot for the nominees, which being done, the newly elected officers were duly installed by the presiding officer, each pledging his earnest support to the Branch, as well as to the parent body.

CHAS. A. APMEYER, Secretary.

The report of the Legislative Committee is as follows:

### REPORT OF THE COMMITTEE ON LEGISLATION OF THE CINCINNATI BRANCH OF THE A. PH. A.

Mr. President and Members:

Your Committee on Legislation begs to report at this annual meeting that during the year there has been no legislation, either state or national, which is of particular con-

cern to pharmacists. There are, however, at this time two bills pending in Congress which are of very special interest, and which will be referred to herein.

The state laws of interest to the various branches of the drug trade which were enacted during the year 1913, and which came to be in force since that time, have been reported on at one of the regular monthly meetings during the year. They included the Agricultural Commission Law, the so-called Duffy Anti-Narcotic Law, an amendment to the Pure Food and Drug Law which declared a drug to be misbranded if labels bear or contain any statement, design or device regarding the curative or therapeutic effect of the article or any of the ingredients or substances contained therein, which *is false and fraudulent,* and finally the Insecticide Law. Since these laws became effective, the Agricultural Commission has taken up the duties which rested heretofore with the Board of Pharmacy and which were transferred to it. There appear to have been many prosecutions on account of the violation of various laws, particularly, however, with reference to the violation of the so-called Duffy Anti-Narcotic Law. While it is too early to express an opinion on the value of this particular work under the direction of the Agricultural Commission, there is but little doubt that the Commission will have many advantages in the proper enforcement of such laws, and consequently conditions should be correspondingly improved. The Duffy Anti-Narcotic Law and its enforcement by the Agricultural Commission has certainly resulted in numerous prosecutions and convictions, and continued determined activity in this respect is bound to be very helpful in the control of the narcotic evil. It, of course, is not possible for your committee to know the merits of the various prosecutions which have been made. In this connection, it is to be regretted that the Agricultural Commission construes the law as being inapplicable to physicians, dentists and veterinarians, at least such is reported to be the case. It is altogether impossible for your committee to understand how the Agricultural Commission would construe this law as not requiring physicians, dentists and veterinarians to write and file prescriptions when they themselves dispense the drugs in question. There seems to be no room for such strained construction under a plain reading of the Narcotic Law, and in keeping with its terms physicians, dentists and veterinarians should be required to write and file prescriptions when they themselves dispense the drug. We at this time recommend that this matter be brought more directly to the attention of the Agricultural Commission, and that they be advised that this Branch of the American Pharmaceutical Association believes the law to be equally applicable to physicians, dentists and veterinarians who make a practice of dispensing. The Insecticide Law, the many uncalled-for provisions of which were brought to the attention of the Branch during the year, has since been attacked in a suit brought under the direction of the Ohio State Pharmaceutical Association, and particularly because of the earnest effort of Prof. Geo. B. Kauffman, the Chairman of its Council. We report with pleasure and satisfaction that the lower court has sustained the contention of the Ohio State Pharmaceutical Association, and has held the law to be unconstitutional because of discriminating features. Upon just what ground the decision of the lower court has been based, we do not yet know, because a publication of the opinion has not yet been available.

In considering state legislation generally, and its enforcement, it is of special interest to know, that an Itinerant Venders' Law of the State of Louisiana, in which the Supreme Court of said state upheld special license features and regulations to govern the sale of drugs by itinerant venders, has on error to the Supreme Court of the United States, been upheld by it. The decision of the Louisiana court, which was under review by the Supreme Court of the United States in this case, seems to be in direct conflict with a decision rendered on a similar law, by the Illinois Court of Appeals. We find, therefore, that the highest courts of two different states have come to different conclusions with reference to the constitutional limitations which govern state legislatures, and while the Supreme Court of the United States has sustained the conviction as made under the Louisiana law, it must be in mind, that the question before the Supreme Court of the United States was simply to decide whether the Louisiana law infringed upon the constitutional rights of citizens of the United States. Of necessity it had to leave to the state court the question as to whether the constitutional limitations of the state had

been infringed, and as already pointed out in this respect, there was a direct conflict in the decision as reached by the Illinois and Louisiana courts respectively. While some weight is added to the Louisiana decision, because of the affirmance of the Supreme Court of the United States, yet the more important question will still remain for independent decision by the several state courts, and the state courts, generally speaking, outside of the Southern States, would be more inclined to follow the decision of the highest court of Illinois than to follow the highest court of the State of Louisiana.

In proposed national legislation, the Harrison Anti-Narcotic Bill continues to be a center of interest on the part of the various branches of the drug trade, no doubt also on the part of the medical profession. The bill is still pending in the Senate of the United States. Fortunately, the National Drug Trade Conference has seen fit to advocate amendments to the bill as first approved by it, which are in keeping with the needs as pointed out by the Cincinnati Convention of the N. A. R. D. In fact, all of the amendments as they were advocated, have found either total or partial approval by the Drug Trade Conference, including the need for record requirement on the part of dispensing physicians, dentists and veterinarians. However, the proposal of the National Drug Trade Conference, with reference to the record requirement to be made of physicians, etc., who dispense and distribute narcotics, is not sufficiently definite and certain, and will not be particularly helpful to control the illegitimate distribution of narcotics by such persons, unless changed, so as to definitely require a record for each separate distribution, other than the administration of the drug by physicians themselves in cases of emergency. It appears that the need for such further change has been pointed out to various Senators, and we may hope somewhat that the change will still be made before the so-called Harrison Bill finally becomes a law. At any rate, it is now possible to say, that some of the much needed changes will surely be embodied in the law, and also that the discrimination as first made and proposed in favor of dispensing physicians has come very generally to be recognized as being improper and as seriously impairing the effectiveness of the intended law.

Another bill now pending in Congress which is of particular interest to all of the various Branches of the Drug Trade is the so-called Stevens Price Maintenance Bill. It is the purpose of this bill to allow the manufacturer of trade-marked or proprietary articles to designate the price at which his products shall be sold to the trade and to the consumer. This bill is an outcome of the continued agitation for legalizing price regulation, as first commenced by the National Association of Retail Druggists. The movement and the support for such legislation has now taken on considerable force, and the public generally, as well as its representatives, are being educated on the need for it, and the advocates of price regulation have certainly made wonderful progress, so that it is now within reason to expect that such legislation will be enacted in some form within a reasonable time. The provisions of the Stevens Bill in singling out trade-marked and proprietary articles, are possibly not so complete as they should be, for there seems to be no good reason why the same rights should not be accorded the manufacturer of a patented or copyrighted article, in view of the fact that the courts have held that the owner of patented or copyrighted articles may not dictate the price at which such articles shall be sold by dealers. There is also some question as to the constitutional right of Congress to enact a law which, beyond the contract provisions, is to govern the owner of property which has come to be under the exclusive jurisdiction of the state as distinguished from interstate. In other words, it is a question, whether when property has come to the exclusive ownership of a resident of a given state he can be denied, beyond the terms of an actual contract, by an act of Congress to dispose of such property as he sees fit. The theory of the Stevens Bill in this respect seems to be based on an assumed analogy with the patent and copyright authority of Congress, and such analogy in fact does not exist. Your committee has not found time to devote special study to this feature, and is not prepared at this time to express a definite opinion with reference to it, but believes it well to call attention to the matter for general consideration. Whatever the case may be, the all-important fact is, that the progress for legalizing price regulation during the year has been most wonderful, and that the public and the legislators are becoming thoroughly im-

pressed with the need for some relief in this respect, and when the campaign of education has sufficiently progressed, there is no doubt about finding some legal and constitutional method for properly taking care of the matter. Respectfully submitted,

WM. C. LAKAMP.
FRANK H. FREERICKS.

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## CHICAGO.

The Chicago Branch met for the last regular monthly meeting of the season at the University of Illinois School of Pharmacy building, the evening of May 19th, with President J. H. Wells in the chair.

Mr. Wells introduced Mr. L. A. Becker, who lead the discussion of the evening on the topic, "The Preparations of the New U. S. P." Mr. Becker made suggestions as to the improvement or correction of several formulas and tests. He criticised the tests for iron in "Aqua," stating that he found the "heavy metals test," of the present Pharmacopœia, more efficient than the proposed test for metals. He said that the proposed test for iron should not read "immediately" but should have a time limit. Iron 1-100,000 required one minute, to develop a positive reaction, 1-500,000 required 3½ to 5 minutes, solutions of 1-1,000,000 showed the color only in 7 to 10 minutes. He pointed out in connection with "Aqua Destillata Sterilisata" and "Liquor Sodii Chloridi Physiologyicus," the necessity for extreme care in sterilization, and recommended, for the latter solution, fractional sterilization, using the autoclave at 115° to 120° for 15 to 20 minutes on three successive days, or boiling for one hour on three successive days. Should the pharmacist become the purveyor of this preparation to the physician, the directions as proposed for sterilization, will lead to many disputes, for where there is infection, from either instruments, dressings, suture materials, or preparations, the physician often seeks to put the blame on any other cause rather than to ascribe bad results to his possibly faulty technique or poor judgment. For the pharmacist's protection against accusations of this nature, the process of sterilization should produce unquestionable results.

Mr. Wm. Gray followed Mr. Becker with the following suggestions:

*Liquor Cresolis Comp.*: Use Sapo Mollis and Cresol equal parts. Dissolve with heat. *Tinct. Iodi*: Use 40 cc. of water to the liter of tincture for insuring solution of the K. I.; *Tinct. Aurantii Dulcis* and *Tinct. Limonis Cortex* Retain the present formula; oil will be lost by grating; *Tinctures in General*: There should be some form of standardized concentrated preparation of the assayed drugs, which could be diluted to make U. S. P. tinctures, for the benefit of pharmacists who cannot afford to make such tinctures with assay process for the same. The present Tincture of Nux Vomica is an example. Otherwise the entire preparation of assayed tinctures is going into the hands of the pharmaceutical manufacturer. The plan proposed would allow considerable saving both in cost of container, menstruum and freight.

A communication was received from Mr. R. E. Rhode, who commented as follows: *Aromatic waters* should be made with magnesia instead of talcum. Recently boiled water may lead to better preparations.

*Solution of Magnesium Citrate* should be made by the cold process, and with Spirit of Lemon, instead of the oil. The proposed process is altogether too complicated for what is practically an extemporaneous preparation and, furthermore, a volatile oil should not be added to a hot liquid. He recommends the return to the use of the name Tr. Saponis Mollis or Spir. Saponis Mollis instead of Linimentum Saponis Mollis.

In the discussion of Mr. Gray's suggestion of "concentrate" for tincture-making, Professor Clark opposed the idea, believing that a druggist using guaranteed assayed drugs, should be educated to prepare U. S. P. tinctures directly from them.

Professor Day suggested that neighborhood-druggists should club together and engage an expert to make the U. S. P. preparations in larger quantities and of standard quality.

Mr. Storer, in commenting on the preparation of Green Soap and Comp. Solution of Cresol, stated that he prepared the soap in 50-pound quantities, with careful manipulation and with not too close an adherence to the formula, and then allowed it to age for three months. From this soap he prepared the Cresol Solution and allowed it to age some months before use. Both preparations were declared to be very satisfactory.

Secretary Gathercoal read a letter from Mr. Fred Meissner, of LaPorte, Trustee of the Pharmacopœia, who stated that the pros-

pects for the new U. S. P. to be in print early this fall were very good indeed.

The annual convention of the Illinois Pharmaceutical Association at Fox Lake, June 11, 12 and 13th, was announced, and a general invitation to be present was issued.

Arrangements for the Chicago delegation to the convention at Detroit were also discussed.

The meeting adjourned until the third Tuesday in October.

E. N. GATHERCOAL, Secretary.

## The Pharmacist and the Law

### NEW YORK ANTI-NARCOTIC LEGISLATION.

The bill known as the Boylan bill, for the regulation of sales of chloral, opium, any of the salts, alkaloids or derivatives of opium, hypodermic syringes or needles, has become a law in the State of New York.

The bill prohibits the sale of these drugs and articles except upon the prescription of a physician, veterinarian or dentist, with the exception of preparations containing minimum quantities of such drugs. The law also provides for the keeping of records by the person prescribing any of the drugs mentioned in the bill, and also for the recording, by every dealer, of the name and the address of every person to whom such drugs or articles are sold. It also provides for the commitment to a hospital or institution of persons proven to be habitual drug-users, and for their detention therein until they are deemed to be cured of their morbid desire. It further provides for the revocation of the license of any pharmacist, physician, veterinarian, dentist or registered nurse, who may be addicted to the abuse of any habit-forming drug, or who has been convicted of violation of any of the provisions of the act, but, while in the first instance, it provides for the reissuance of a license on the reformation of the habits of a habitual drug-user, the revocation of a license after conviction, seems to be intended to be of permanent continuance, not subject to a revision. The full text of the bill follows:

AN ACT TO AMEND THE PUBLIC HEALTH LAW, IN RELATION TO THE SALE OF HABIT-FORMING DRUGS.

The People of the State of New York, represented in Senate and Assembly, do enact as follows:—

Section 1. Chapter 49 of the laws of 1909, entitled "An act in relation to the public health, constituting chapter 45 of the consolidated laws," is hereby amended by adding after article 11 a new article to be article 11a thereof, to read as follows:—

ARTICLE 11a.

Habit-Forming Drugs.

Sec. 245. Sale prohibited; exception. No pharmacist, druggist or other person shall sell, have or offer for sale or give away any chloral, opium or any of its salts, alkaloids or derivatives, or any compound or preparation of any of them except upon the written prescription of a duly licensed physician, veterinarian or dentist, provided that the provisions of this article shall not apply to the sale of domestic and proprietary remedies, actually sold in good faith as medicines and not for the purpose of evading the provisions of this article, and provided further that such remedies and preparations do not contain more than two grains of opium or one-fourth grain of morphine or one-fourth grain of heroin or one grain of codeine or ten grains of chloral or their salts in one fluid ounce, or if a solid preparation, in one avoirdupois ounce, nor to plasters, liniments and ointments for external use only.

Sec. 246. Prescriptions; certificates. It shall be unlawful for any person to sell at retail or give away any of the drugs, their salts, derivatives or preparations mentioned in section 245 of this chapter, except as herein provided without first receiving a written prescription signed by a duly licensed physician, veterinarian or dentist. The prescription must contain substantially the following:—The name in full of the physician, veterinarian or dentist issuing such prescription, his office address, his office hours and telephone, and the name, age and address of the person to whom and date on which such prescription is issued. It shall be unlawful for any duly licensed physician, veterinarian or dentist to issue any such prescription containing any of the drugs, their salts, derivatives or preparations mentioned in section 245 of this chapter except after a physical examination of any person for the treatment of disease, injury or deformity. It shall be unlawful for any person to sell at retail any of the drugs or preparations of any of those mentioned in section 245 of this article without first verifying the authority of any prescription containing more than four grains of morphine, thirty grains of opium, two grains of heroin, six grains of codeine or four drams of chloral. Such veri-

fication can be made by telephone or otherwise. Such prescription so received shall be filled out at the time of receiving the same for the full quantity prescribed and no prescription so received shall be filled out more than ten days after the date which said prescription be dated. Such prescription, from which no copy shall be taken, shall be retained by the person who dispenses the same and shall be filled but once. Such prescription shall be kept on the general prescription file and given a regular consecutive number on such file. On such prescription shall be inscribed the name and address of the purchaser making such purchase and the date upon which said sale is made. Any person who sells at retail, furnishes or dispenses any of the drugs mentioned in section 245 of this chapter upon a written prescription by a duly registered physician or veterinarian or dentist shall at the time of dispensing the same, place upon the package a label or deliver therewith a certificate stating the name and address of the person selling or furnishing the same, the name and the address of the physician, veterinarian or dentist upon whose prescription such sale is made, the date of sale, and the name of the person to whom such sale is made. Any person, other than a manufacturer of any of the drugs mentioned in section 245 or a wholesale dealer in drugs or a licensed pharmacist, licensed druggist, duly registered practicing physician, licensed veterinarian or a licensed dentist, who shall possess any of the drugs mentioned in section 245 or their salts, derivatives or preparations, shall be guilty of a misdemeanor, unless said possession is authorized by the certificate described in this section.

Nothing herein contained shall be construed to prohibit the sale of any of such drugs by any manufacturing pharmacists or chemists, or wholesale or retail pharmacists, or druggists, to other manufacturing pharmacists or chemists, or wholesale or retail pharmacists, or druggists, or to hospitals, colleges, scientific or public institutions, except that such sales shall be made in the manner provided in the next succeeding section.

Sec. 247. Order blanks; filing. The State Commissioner of Health shall prepare and furnish to all Boards of Health or officers official order blanks, serially numbered in duplicate, bound in book form, with carbon or transfer paper between the duplicate pages. The said official order shall be furnished by the local Health Board or officer to any local, duly licensed physician, dentist, pharmacist, druggist or veterinarian, upon which must be written all orders for the purchase of any of the drugs enumerated in section 245 of this chapter for the use of such physician, dentist, pharmacist, druggist or veterinarian. It shall be unlawful for any person to sell, furnish or dispose to any physician, pharmacist, druggist, veterinarian or dentist any of the drugs enumerated in section 245 of this chapter without first receiving from such physician, druggist, veterinarian or dentist an official order blank as provided in this section, which official order shall be retained by the person or corporation who sells, furnishes or dispenses any of the drugs enumerated in section 245 of this chapter, and such official order shall be kept in a separate file or book and an entry made or caused to be made on the order stating the date of sale, the name and address of the purchaser and the name of the person making such sale.

Sec. 248. Physicians, etc., to keep records. All physicians, druggists, pharmacists, veterinarians and dentists shall keep on record the name and address of each person to whom such physician, dentist or veterinarian administers or disposes in any way whatsoever any of the drugs enumerated in section 245 of this chapter, and the quantity so administered, disposed of or given away. Such record shall be preserved for five years and shall always be open for inspection by the proper authorities. Any violation of this section is hereby declared to be a misdemeanor.

Sec. 249. Hypodermic syringe; sale of; record; penalty. It is unlawful for any person to sell at retail or to furnish to any person other than a duly licensed physician, dentist or veterinarian, an instrument commonly known as a hypodermic syringe or an instrument commonly known as a hypodermic needle, without the written order of a duly licensed physician or veterinarian. Every person who disposes of or sells at retail, or furnishes or gives away to any person, either of the above instruments, upon the written order of a duly licensed physician or veterinarian, shall, before delivering the same, enter in a book kept for that purpose the date of the sale, the name and address of the purchaser, and a description of the instrument sold, disposed of, furnished or given away. Any person or persons who sell, dispose of or give away an instrument commonly known as a hypodermic syringe, or an instrument commonly known as a hypodermic needle, except in the manner prescribed in this section, shall be guilty of a misdemeanor.

Sec. 249-a. Commitment of habitual drug users; procedure; discharge. The constant use by any person of any habit-forming drug, except under the direction and consent of a duly licensed physician, is hereby declared to be dangerous to the public health. Whenever a complaint shall be made to any magistrate that any person is addicted to the use of any habit-forming drug, without the consent or direction of a duly licensed physician, such magistrate, after due notice and hearing, is satisfied that the complaint is founded and that the person is addicted to the use of a habit-forming drug, shall commit such person to a state, county or city hospital or institution licensed under the State Lunacy Commission. Whenever the chief medical officer of such institution shall certify to any magistrate that any person so committed has been sufficiently treated or give any other reason which is deemed adequate and sufficient, he may discharge the person so committed. Every person committed under the provisions of this section shall observe all the rules and regula-

tions of the institution or hospital. Any such person who wilfully violates the rules and regulations of the institution or repeatedly conducts himself in a disorderly manner may be taken before a magistrate by the order of the chief medical officer of the institution. The chief medical officer may enter a complaint against such person for disorderly conduct and the magistrate, after hearing and upon due evidence of such disorderly conduct, may commit such person for a period of not to exceed six months to any institution to which persons convicted of disorderly conduct or vagrancy may be committed, and such institution shall keep such persons separate and apart from the other inmates, provided that nothing in this section shall be construed to prohibit any person committed to any institution under its provisions from appealing to any court having jurisdiction for a review of the evidence in which this commitment was made.

Sec. 249-b. Revocation of licenses. Any license heretofore issued to any physician, dentist, veterinarian, pharmacist or registered nurse may be revoked by the proper officers or boards having power to issue licenses to any of the foregoing upon proof that the licensee is addicted to the use of any habit-forming drug or drugs after giving such licensee reasonable notice and opportunity to be heard. Whenever it shall appear after one year from date of revocation of such license that such licensee has fully recovered and is no longer an addict to any of the drugs herein prohibited, such board may grant a rehearing and in its discretion reissue the license of such licensee.

Sec. 249-c. Revocation of license after conviction. Whenever any physician, dentist, veterinarian, pharmacist or registered nurse is convicted in a court having jurisdiction of any of the violations of this article, any officer or board having power to issue licenses to any such physician, dentist, veterinarian, pharmacist or registered nurse may, after giving such licensee reasonable notice and opportunity to be heard, revoke the same.

Sec. 249-d. Penalties. Any violation of any of the provisions of this article shall be deemed a misdemeanor. Nothing contained in this article shall be construed to amend or repeal section 1746 of the penal law.

Sec. 2. This act shall take effect July 1, 1914.

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## FOOD INSPECTION DECISION NO. 153.

AMENDMENT TO REGULATION 9, RELATING TO GUARANTIES BY WHOLESALERS, JOBBERS, MANUFACTURERS, AND OTHER PARTIES RESIDING IN THE UNITED STATES TO PROTECT DEALERS FROM PROSECUTION.

Regulation 9, of the Rules and Regulations for the enforcement of the Food and Drugs Act, June 30, 1906 (34 Stat., 768), is hereby amended, effective May 1, 1915, so as to read as follows:

REGULATION 9. GUARANTY.
(Section 9.)

(a) It having been determined that the legends "Guaranteed under the Food and Drugs Act, June 30, 1906," and "Guaranteed by (name of guarantor), under the Food and Drugs Act, June 30, 1906," borne on the labels or packages of food and drugs, accompanied by serial numbers given by the Secretary of Agriculture, are each misleading and deceptive, in that the public is induced by such legends and serial numbers to believe that the articles to which they relate have been examined and approved by the Government and that the Government guarantees that they comply with the law, the use of either legend, or any similar legend, on labels or packages should be discontinued. Inasmuch as the acceptance by the Secretary of Agriculture for filing of the guaranties of manufacturers and dealers and the giving by him of serial numbers thereto contribute to the deceptive character of legends on labels and packages, no guaranty in any form shall hereafter be filed with and no serial number shall hereafter be given to any guaranty by the Secretary of Agriculture. All guaranties now on file with the Secretary of Agriculture shall be stricken from the files, and the serial numbers assigned to such guaranties shall be canceled.

(b) The use on the label or package of any food or drug of any serial number required to be canceled by paragraph (a) of this regulation is prohibited.

(c) Any wholesaler, manufacturer, jobber, or other party residing in the United States may furnish to any dealer to whom he sells any article of food or drug a guaranty that such article is not adulterated or misbranded within the meaning of the Food and Drugs Act, June 30, 1906, as amended.

(d) Each guaranty to afford protection shall be signed by, and shall contain the name and address of, the wholesaler, manufacturer, jobber, dealer, or other party residing in the United States making the sale of the article or articles covered by it to the dealer, and shall be to the effect that such article or articles are not adulterated or misbranded within the meaning of the Federal Food and Drugs Act.

(e) Each guaranty in respect to any article or articles should be incorporated in or attached to the bill of sale, invoice, bill of lading, or other schedule, giving the names and quantities of the article or articles sold, and should not appear on the labels or packages.

(f) No dealer in food or drug products will be liable to prosecution if he can establish that the articles were sold under a guaranty given in compliance with this regulation.

W. G. McADOO,
Secretary of the Treasury.
D. F. HOUSTON,
Secretary of Agriculture.
WILLIAM C. REDFIELD,
Secretary of Commerce.

Washington, D. C., May 5, 1914.

## Council Business

COUNCIL LETTER No. 17.

PHILADELPHIA, PA., April 21, 1914.

To the Members of the Council:

The following letter has been received by the Secretary of the Council from President George M. Beringer:

"I have been giving very earnest thought to Council Letter No. 16 and the communication presented therein from General Secretary and Editor James H. Beal. Since you communicated with me over the telephone the receipt of this letter of Dr. Beal, the matter has weighed very heavily upon me.

There is no question but what Dr. Beal's health must be conserved and that the Association is confronted with the necessity of relieving him at an early date from his position as Secretary and Editor. The necessity is for a most careful canvass of the field and the selection of the proper person or persons for these two offices is one of great importance to the Association. With the enlarged activities of the A. Ph. A. it is going to be exceedingly difficult for any one person to successfully fill both of these positions. It would be difficult to find in one individual all the qualifications that are required. Our previous Secretaries have set a very high mark for this position and the standing of the American Pharmaceutical Association as the exponent of American pharmacy demands that this standard shall be maintained.

Personally, I am strongly averse to the acceptance of the resignation of Dr. Beal as Editor and Secretary in the manner in which it is proposed to be done by Motion No. 28. I would like to see Dr. Beal retained as Secretary and Editor at least until the Detroit meeting. His name should be continued as the Editor and General Secretary until that time, even though his services in the interim be merely nominal. I believe that the Association can very well afford to assume this position. The work done by Dr. Beal as Secretary as well as his other work in behalf of the Association has endeared him to every member and merits at least this small recognition. The Association does not want to be left even temporarily without a Secretary, even though his connection be nominal.

If it is in order, I would move as a substitute for the two motions Nos. 28 and 29:

First—That the resignation of Dr. James H. Beal as Editor and Secretary be accepted with the sincere regret of the Council and with the understanding that such resignation shall not take effect until September 1, 1914.

Secondly—That Dr. James H. Beal be relieved of the active work of the Secretaryship and Editorship of the JOURNAL as far as possible and that he be authorized to make the best arrangements he can with Mr. Ernest C. Marshall or other person or persons that he may select, to carry on the work of the offices of Secretary and Editor under his direction until September 1st.

This would enable Dr. Beal to make the best arrangements for his personal comfort and with the least interruption of the work of the Association."

The first substitute motion will be known as *Motion No.* 30, and the second as *Motion No.* 31.

Dr. Beal has been communicated with in reference to above, and signifies his willingness to retain the *nominal* title of Editor and General Secretary until September 1st; provided, however, that somebody can be designated as *Acting Secretary and Editor,* to whom business matters addressed to him can be referred.

J. W. ENGLAND,
Secretary of the Council.

415 N. Thirty-third Street.

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COUNCIL LETTER No. 18.

PHILADELPHIA, PA., April 28, 1914.

To the Members of the Council:

*Motion No.* 27 (*Election of Members; Applications Nos.* 91 *to* 123 *inclusive*), and *Motions No.* 30 (*Accepting Resignation of Dr. James H. Beal as Editor and General Secretary*), and *No.* 31 (*Authorizing Dr. James H. Beal to engage a person or persons to carry on the work of the offices of Editor and General Secretary until September* 1; *substitute motions for Motions No.* 28 *and No.* 29), have each received a majority of affirmative votes.

The following letter has been received by the Secretary of the Council from President George M. Beringer:

"I am sending you herewith a letter received under date of April 20th from the Drug Products Co., Inc. Will you kindly include this communication in an early Council letter?"

The letter referred to is as follows:

"Mr. G. M. Beringer, President, American Pharmaceutical Association, 501 Federal St., Camden, N. J.:

Dear Mr. Beringer—Confirming recent conference with yourself, Mr. F. M. Apple, Mr. J. R. Muir and the writer, in the interest of the public welfare and the retail drug trade, we shall be pleased to co-operate with the efforts of the American Pharmaceutical Association to have the coffin-shaped Bichloride of Mercury Tablet adopted as the official design or shape for this poisonous tablet, and, to encourage and further such a

movement we will be willing to assign our exclusive rights and claims, including application for patent, to the American Pharmaceutical Association.

We also wish to confirm the writer's contention made to you in person, namely, that he regards himself as the inventor and originator of the coffin-shaped Bichloride of Mercury Tablet and can present proof that it was his intention to market such a tablet prior to the existence or incorporation of the Drug Products Co., Inc., to whom the claim has been assigned.

We direct your attention to the date of patent office letter of acknowledgment of our application for patent which is September 2, 1913, No. 787813, and also date of application for similar patent as stated in correspondence to you from The Norwich Pharmacal Company which is given as November 18, 1913, No. 801748! This in itself indicates prior right on our part. It is also a fact that our advertisement of this tablet was the first to appear in any of the papers in this country, and it is a further fact that the tablets we are marketing to-day are precisely as they have been from the beginning, with POISON on one side and skull and crossbones on the other, while the tablets as marketed today by The Norwich Pharmacal Company are not the same with respect to embellishments as marketed by them previously.

The Commissioner of Patents has denied our application for patent on the grounds that it is lacking in patentable novelty, in view of what is shown in design patent 20135, Booth, September 9, 1890—bottles and figures, however, if there is any possibility of amending the present application or in formulating a new joint application for a design patent to be assigned to the American Pharmaceutical Association we will gladly join with Mr. Franklin M. Apple and any others who may have any rights in the matter. We also shall be pleased to encourage and support proper legislation to make the coffin-shaped the sole type for Bichloride of Mercury antiseptic tablets and to restrict this design or shape to that purpose only. As a matter of fact, we have taken considerable interest in this phase of the question and have communicated and corresponded with members of the Legislature in several of the different States.

Thanking you for the courtesy which you have already displayed and awaiting your further valued advice, we remain,

Cordially yours,
THE DRUG PRODUCTS CO., INC.,
H. NOONAN, President.

New York, April 20, 1914."

The following communication has been received from George M. Beringer, Chairman of the Committee on Unofficial Standards, under date of April 25, 1914:

"At the Nashville meeting, the Committee on Unofficial Standards was instructed to forward to the Editor of the JOURNAL the monographs for standards, when tentatively adopted, for publication in the JOURNAL, and to make a report on same to the Council.

In compliance with this instruction, I will report for the Committee that we have forwarded to Editor Beal monographs on the following subjects:

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|---|---|
| Agaricus | Amari Corticis |
| Albumen Ovi Recens | Oleum Aurantii Florum |
| Asclepias | Oleum Bergamottæ |
| Baptisia | Oleum Myrciæ |
| Delphinium | Ovum Gallinaceum |
| Dioscorea | Passiflora |
| Fraxinus | Pumex |
| Fructus Rubi | Sambucus |
| Fructus Rubi Idaei | Senecio |
| Fructus Solani Carolinensis | Strontii Carbonas |
| Gemmæ Populi | Succus Citri |
| Juglans | Succus Pomorum |
| Juniperus | Trifolium |
| Lac Vaccinum | Trillium |
| Menyanthes | Verbena |
| Oleum Aurantii | Vitellum Ovi Recens." |

The following communication has been received:

"Mr. J. W. England, Secretary, Council A. Ph. A., Philadelphia, Pa.:

Dear Sir—At a meeting of members of the American Pharmaceutical Association residing in San Francisco and vicinity the organization of a San Francisco Branch was proposed. It was decided to petition the Council for permission to permanently organize. I am enclosing a petition asking that permission.

The proposed Branch will meet on the second Tuesday of the month. The next meeting has been called for May 12th, 723 Pacific Building, San Francisco. I do not know the exact procedure to become officially recognized, but I hope we may organize permanently on that evening.

Very truly yours,
(Signed) CLARISSA M. ROEHR,
Secretary *pro tempore.*

San Francisco, April 17, 1914."

To the Council of the American Pharmaceutical Association

We, the undersigned, members of the American Pharmaceutical Association, respectfully petition your honorable body to permit the establishment of a local Branch to be known as the San Francisco Branch of the American Pharmaceutical Association:

Val. Schmidt, 1845 Polk St.
S. A. Sharp, 1845 Polk St.
H. L. McDonnell, S. E. Cor. Powell and Geary Sts.
Claude T. Headen, 201 Frederick St.
John H. Dawson, 2489 Howard St.
Stewart McGee, 1635 Julia St.
J. G. Munson, 54 N. 5th St., San Jose.
Edward F. Varney, 1301 Broadway, Oakland.
R. A. Leet, 1301 Broadway, Oakland.
Frank T. Green, 500 Devisadero St.

H. B. Carey, 1294 7th Ave.
Arthur Reum, 1291 Stanyon St.
Albert Schneider, 723 Pacific Bldg.
T. L. Lengfeld, 1350 Sutter St.
J. M. White, 416 Hayes St.
A. A. Poehner, 1515 Golden Gate Ave.
Tony Prior, 282 San Jose Ave.
James H. Winter, 1375 Valencia St.
Carl F. Stange, 1400 18th St.
Westersvon Krakan, 2801 Bryant St.
J. H. Flint, 2489 Howard St.
David H. Fletcher, 3993 Washington St.
Philomena M. N. Goodman, 3163 Mission St.
J. W. Boyken, 2574 Mission St.
Henry M. Donahue, 2290 Market St.
John Zieg, 35 Second St.
Clarissa M. Roehr, University Hospital.

*Motion No.* 32 (*Organization of San Francisco Branch, A. Ph. A.*). Do you approve of the organization of the San Francisco Branch of the American Pharmaceutical Association?

J. W. ENGLAND,
Secretary of the Council.
415 N. Thirty-third Street.

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## COUNCIL LETTER No. 19.

PHILADELPHIA, PA., April 30, 1914.

To the Members of the Council:

The following letter has been received from President George M. Beringer:

"CAMDEN, N. J., April 28, 1914.

To the Council of the American Pharmaceutical Association:

Gentlemen—There has arisen a situation in respect to the Section on Commercial Interests that I believe is without precedent and is not covered by the by-laws.

At the Nashville meeting, Mr. Gus Lindvall was elected Chairman of this Section. On March 26th, Mr. Lindvall wrote to the President that he had sold out his drug business in 1913 and had planned a trip abroad and would not be present at the Detroit meeting. He was of the opinion that his Associates, because of other duties or uncertainty of attending the meeting, were not in a position to assume the chairmanship of the Section and prepare the necessary programs. On April 9th, Mr. Lindvall wrote to your President tendering his resignation.

Immediately on receipt thereof, your President engaged in correspondence with the Secretary of this Section and the Associates elected at the Nashville meeting. There was no time to lose if a satisfactory program was to be arranged for the sessions of the Section at the Detroit meeting as provided for in the program. As the result of our correspondence and at the request of the Associates, Mr. Harry B. Mason has consented to accept the chairmanship of this Section. I am pleased to make this appointment subject, of course, to the approval of the Council. In the absence of a precedent, I am not sure of the authority of the President to fill such vacancies, but assume that my action in this matter will meet with the approval of the Council.

Mr. Mason's recognized ability and energy and his past work in behalf of the Association bespeak a good program and successful meetings of this Section at Detroit. Mr. Mason's appointment as Chairman of this Section, doubtless, will carry with it his appointment as an ex-officio member of the Council the same as that of other Chairmen of Sections. Yours sincerely,

GEORGE M. BERINGER, President."

*Motion No.* 33 (*Approval of Appointment of Harry B. Mason as Chairman of Committee on Commercial Interests*). Do you approve appointment of Harry B. Mason as Chairman of Committee on Commercial Interests?

J. W. ENGLAND,
Secretary of the Council.
415 N. Thirty-third Street.

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## COUNCIL LETTER No. 21.

Philadelphia, Pa., May 22, 1914.

To the Members of the Council:

The following communications have been received from Julius A. Koch:

PITTSBURGH, May 15, 1914.

Prof. Julius A. Koch, Pittsburgh College of Pharmacy, Pittsburgh, Pa.:

DEAR SIR—We have duly received your letter of May 9th and in accordance therewith and in keeping with our previous letter, we enclose herewith a formal assignment of a patent on Antiseptic Leaves to the American Pharmaceutical Association.

This assignment is made absolute as in the case of the coffin-shaped tablet. We understand that it will only be effective so far as the Association is concerned provided this form is made official.

We would also like to suggest that so far as it may be practical, the Association use its efforts to secure a price maintenance plan on the sale of this article for the benefit of the pharmacists of the country, for were we to continue in the exclusive manufacture, we would endeavor to protect the retail druggist so far as the legal limitations would permit.

We are glad to place this article in the hands of the Association and hope that our action may be of value to the pharmaceutical world at large. Very truly yours,

THE WM. S. MERRELL CHEMICAL CO.,
CHARLES F. MERRELL.

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"ASSIGNMENT."

WHEREAS, Charles G. Merrell and R. W. Proctor, both citizens of the United States, residing at Cincinnati, in the County of Hamilton and State of Ohio, have invented a new,

original, and useful improvement in packages for Antiseptic Poisons, for which they made application for letters patent, which was filed in the United States Patent Office upon February 7, 1914, and serially numbered 817,364; and

WHEREAS, The Wm. S. Merrell Chemical Company, Inc., duly incorporated under the laws of the State of Ohio, and doing business at Cincinnati, in the County of Hamilton and State of Ohio, has acquired the entire interest in said invention and in and to the letters patent of the United States to be obtained therefor; and

WHEREAS, The American Pharmaceutical Association, Inc., duly incorporated under the laws of the State of* ————————, and doing business at ————————, in the County of ————————, and State of ————————, is desirous of acquiring an interest in said invention and in and to the letters patent of the United States to be obtained therefor. Now, therefore,

Be it known that for and in consideration of the sum of one dollar, to us in hand paid, the receipt of which is hereby acknowledged, and other valuable consideration, the said The Wm. S. Merrell Chemical Company, have sold, assigned and set over, and do by these presents hereby sell, assign and set over unto the said American Pharmaceutical Association, Inc., its successors and assigns, the entire right, title and interest in and to the said design and in and to the letters patent of the United States which may be granted therefor; and we do hereby authorize and request the Commissioner of Patents to issue the said letters patent to the said American Pharmaceutical Association, Inc., in accordance with this assignment.

In testimony whereof, we have hereunto set our hand and affixed our seal this ——— day of ———, 1914.

(Signed) GEORGE MERRELL,
President.

Witnesses: Charles H. Busch.

J. W. ENGLAND,
Secretary of the Council.

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COUNCIL LETTER No. 22.

Philadelphia, May 22, 1914.

To the Members of the Council:

The following program for the sixty-second annual meeting of the American Pharmaceutical Association, to be held at Detroit, Mich., August 24-29, 1914, is submitted:

*Program for the Sixty-second Annual Meeting.*

*Monday.*

9:00 a. m. Meeting of the Council.
3:00 p. m. House of Delegates.
7:30 p. m. First General Session.
Meeting of the Committee on Nomination.
9:30 p. m. Joint Reception of the Presidents of the A. Ph. A. and M. S. P. A.

*Tuesday.*

9:30 a. m. Second General Session.
9:30 a. m. First General Session M. S. P. A.
10:00 a. m. National Association of Boards of Pharmacy.
10:00 a. m. Ladies' Shopping and Visiting, etc.
2:00 p. m. National Association of Boards of Pharmacy.
2:30 p. m. Women's Section.
Scientific Section.
Joint Session of Commercial Section and M. S. P. A.
7:30 p. m. House of Delegates.
7:30 p. m. Meeting of the Council.
8:30 p. m. Conference of Pharmaceutical Faculties.

*Wednesday.*

9:30 a. m. Section on Education and Legislation.
9:30 a. m. Pharmacopœias and Formularies.
10:00 a. m. National Association of Boards of Pharmacy.
12:30 p. m. Luncheon of College Alumni.
2:00 p. m. National Association of Boards of Pharmacy.
2:30 p. m. Section of Practical Pharmacy and Dispensing.
2:30 p. m. Scientific Section.
7:30 p. m. Meeting of the Council.
7:30 p. m. Ladies' Reception.

*Thursday.*

9:30 a. m. Section on Education and Legislation.
Scientific Section.
Joint Session of Practical Pharmacy and M. S. P. A.
10:00 a. m. National Association of Boards of Pharmacy.
1:30 p. m. Excursion.

*Friday.*

9:30 a. m. Historical Pharmacy.
Section on Pharmacopœias and Formularies.
Women's Section.
Commercial Section.
2:30 p. m. Automobile Ride.

*The American Pharmaceutical Association was incorporated at Washington, D. C., February 21, 1888.

7:30 p. m. Re-organization Meeting of the Council.
8:00 p. m. House of Delegates.
8:00 p. m. Ladies' Reception.
8:30 p. m. Joint Session of the Section on Education and Legislation, the A. C. P. F., and the N. A. B. P.

*Saturday.*

9:00 a. m. Meeting of the Council.
10:30 a. m. Final General Session.

Do you approve the above program? This will be regarded as *Motion No. 35 (Approval of Program for 1914 Annual Meeting.)*

J. W. ENGLAND,
Secretary of the Council.

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## UNITED STATES PUBLIC HEALTH SERVICE.

List of Changes of Stations and Duties of Commissioned and Other Officers of the United States Public Health Service for the Seven Days Ended April 22, 1914.

Rucker, W. C., Assistant Surgeon-General. Directed to proceed to Sandy Springs, Md., April 21, 1914, and to Rockville, Md., May 5, 1914, for the purpose of delivering lectures on "Rural Sanitation." April 17, 1914.

Carter, H. R., Senior Surgeon. Detailed to represent the Service at a meeting of the Section for the Eradication of Malaria of the Drainage Congress, to be held at Savannah, Ga., April 22, 1914. April 20, 1914.

Brooks, S. D., Senior Surgeon. Granted 6 days' leave of absence from April 18, 1914. April 17, 1914.

Williams, L. L., Surgeon. Directed to instruct an officer under his charge to proceed to East Hampton, N. Y., not later than April 19, 1914, for special temporary duty. April 18, 1914.

Cobb, J. O., Surgeon. Detailed to attend the meeting of the American Nurses' Association, to be held in St. Louis, Mo., April 23, 1914, and present a paper on "The Potential Influence of the Nurse in the Health of the Nation." April 14, 1914.

Guiteras, G. M., Surgeon. Directed to proceed to Havana, Cuba, for period not to exceed one week, to study plague situation and measures in force for its eradication. April 18, 1914.

Perry, J. C., Surgeon. Granted 46 days' leave of absence, with pay, from April 14, 1914, and 12 months' leave of absence, without pay, from May 30, 1914, with permission to go beyond the seas. April 15, 1914.

Nydegger, J. A., Surgeon. Directed to proceed to the Immigration Station, Ellis Island, N. Y., when most convenient, and remain for a few days, for the purpose of witnessing the various tests there used for the determination of mental development. April 18, 1914.

Gardner, C. H., Surgeon. Granted two days' leave of absence from April 17, 1914, under paragraph 193, Service Regulations. April 17, 1914.

Lavinder, C. H., Surgeon. Relieved from duty in charge of the Marine Hospital at Savannah, Ga., and directed to proceed to Ellis Island, N. Y., and report to the Chief Medical Officer for duty. April 6, 1914.

von Ezdorf, R. H., Surgeon. Directed to extend the work of investigations and studies of malaria so as to include the states of Kentucky, North Carolina, Oklahoma, Tennessee, and Texas. April 15, 1914.

Corput, G. M., Surgeon. Detailed at the request of the President of the State Board of Health of Louisiana, to attend the meetings of the Louisiana State Health Officers, the Louisiana State Medical Association, and the Conference for the Betterment of Health Among Negroes, to be held in New Orleans, La., April 20-25, 1914. April 18, 1914.

Ramus, Carl, Surgeon. Granted 12 days' leave of absence, on account of sickness, from April 10, 1914. April 18, 1914.

Schereschewsky, J. W., Surgeon. Directed, after having completed the necessary steps preliminary to the investigation into the sanitary condition of the garment workers' trade and the physical status of the employes engaged therein in New York, N. Y., to return to Washington, D. C., for preliminary work in regard to methods for the determination of the presence of noxious gases in the air, and in connection with hygienic conditions of illumination. April 15, 1914.

Glover, M. W., Surgeon. Granted 16 days' leave of absence, on account of sickness, from March 23, 1914. April 18, 1914.

Pierce, C. C., Surgeon. Directed to proceed to Gaithersburg, Md., April 17, 1914, and to Brookville, Md., May 12, 1914, for the purpose of delivering lectures on "Rural Sanitation." April 17, 1914.

de Valin, Hugh, Passed Assistant Surgeon. Directed to proceed to Laytonville, Md., May 8, 1914, and to Silver Springs, Md., May 15, 1914, for the purpose of delivering lectures on "Rural Sanitation." April 17, 1914.

Preble, Paul, Passed Assistant Surgeon. Directed, upon receipt of instructions from the officer in charge of the investigation of the pollution of the Ohio River, to proceed to Cincinnati, Ohio, to familiarize himself with the organization, scope, and plans of the investigation. April 14, 1914.

Thometz, H. M., Assistant Surgeon. Granted one day's leave of absence *en route* to Seattle, Wash. April 15, 1914.

Galloway, T. C., Assistant Surgeon. Directed to report to commanding officer of the revenue cutter "Unalga" at San Francisco,

Cal., for duty on summer cruise in Alaskan waters. April 1, 1914.

Porter, J. Y., Quarantine Inspector. Directed to proceed to Havana, for conference with Cuban authorities relative to plague infection at that port. April 20, 1914.

Willetts, David C., Technical Assistant. Directed to proceed via Washington, D. C., to Milledgeville, Ga., for duty in field investigations of the public health. April 20, 1914.

La Grange, J. V., Pharmacist. Granted one day's leave of absence, April 16, 1914. April 15, 1914.

CASUALTY.

Acting Assistant Surgeon B. F. Duke died at Pascagoula, Miss., April 7, 1914.

BOARDS CONVENED.

Boards of medical officers convened to meet Monday, April 27, 1914, at 10 o'clock a. m., for the physical examination and the presentation of questions for the mental examination of candidates for appointment as Assistant Surgeons in the Public Health service, as follows:

Marine Hospital, Stapleton, N. Y.
Detail for the board:
Senior Surgeon G. W. Stoner, chairman.
Assistant Surgeon C. P. Knight, recorder.

Marine Hospital, San Francisco, Cal.
Detail for the board:
Surgeon R. M. Woodward, chairman.
Surgeon J. M. Holt, recorder.

Marine Hospital, Chicago, Ill.
Detail for the board:
Surgeon J. O. Cobb, chairman.
Assistant Surgeon Jos. Bolten, recorder.

Marine Hospital, Chelsea, Mass.
Detail for the board:
Surgeon H. W. Wickes, chairman.
Passed Assistant Surgeon G. L. Collins, recorder.

Marine Hospital, St. Louis, Mo.
Detail for the board:
Surgeon M. J. White, chairman.
Acting Assistant Surgeon H. C. Wakefield, recorder.

Marine Hospital, New Orleans, La.
Detail for the board:
Assistant Surgeon T. J. Liddell, chairman.
Assistant Surgeon C. V. Akin, recorder.
April 18, 1914.

Board convened for re-examination of alien Jacob Weguschin, landed from steamship "Main," to meet at Baltimore, Md., on call of the chairman.

Detail for the Board:
Senior Surgeon H. R. Carter, chairman.
Surgeon J. A. Neydegger, member.
Assistant Surgeon C. E. Waller, recorder.
April 15, 1914.

Official: RUPERT BLUE,
Surgeon-General.

List of Changes of Stations and Duties of Commissioned and Other Officers of the United States Public Health Service for the Seven Days Ended April 29, 1914.

Rucker, W. C., Assistant Surgeon-General. Directed to proceed to Baltimore, Md., for the purpose of delivering an address before the Merchants' and Manufacturers' Association on the subject of typhoid fever, April 28, 1914, at 8 o'clock p. m. April 27, 1914.

Banks, C. E., Senior Surgeon. Directed to proceed to Manitowoc, Wis., for the purpose of making an investigation of the water system of the steamer "Iowa" and advising with officials of the Goodrich Line. April 24, 1914.

Guiteras, G. M., Surgeon. Upon the request of the Secretary of the Navy, approved by the President, April 21, 1914, directed to proceed to Vera Cruz, Mexico, and report to the commander-in-chief of the fleet for such duty as he may assign. April 24, 1914.

Detailed as medical officer of the port of Vera Cruz, Mexico. April 28, 1914.

Wickes, H. W., Surgeon. Authorized, when occasion arises, to direct one of the officers engaged in immigration work at Boston, Mass., together with a clerk, if necessary, to proceed to New Bedford, Mass., to assist in the examination of arriving immigrants. April 24, 1914.

von Ezdorf, R. H., Surgeon. Upon the request of the Secretary of the Navy, approved by the President, April 21, 1914, directed to proceed to Vera Cruz, Mexico, and report to the commander-in-chief of the fleet for such duty as he may assign. April 24, 1914.

Fox, Carroll, Surgeon. Granted one day's leave of absence, April 14, 1914. April 18, 1914.

Goldberger, Jos., Surgeon. Directed to inspect such insane asylums and other institutions and localities in Georgia, Alabama, Florida, Kentucky and other southern states as may be necessary to inaugurate studies of institutional prevalence of pellagra and its cause. April 22, 1914.

Gwyn, M. K., Surgeon. Granted two days' leave of absence on account of sickness, April 9-10, 1914. April 24, 1914.

Schereschewsky, J. W., Surgeon. Granted 10 days' leave of absence from April 17, 1914. April 28, 1914.

Pierce, C. C., Surgeon. Directed to proceed to Germantown, Md., April 24, 1914, for the purpose of delivering a lecture on "Rural Sanitation." April 24, 1914.

Warren, B. S., Surgeon. Granted 5 days' leave of absence returning to station from New Orleans, La. April 22, 1914.

Smith, F. C., Passed Assistant Surgeon. Detailed to represent the Service at the meeting of the National Association for the Prevention and Study of Tuberculosis, to be held in Washington, D. C., May 7-9, 1914. April 27, 1914.

Simpson, Friench, Passed Assistant Surgeon. Granted 5 days' leave of absence from April 13, 1914. April 24, 1914.

Krulish, E., Passed Assistant Surgeon. Granted 24 days' leave of absence *en route* to Juneau, Alaska. April 21, 1914.

Jones, W. M., Assistant Surgeon. Directed to report to the commanding officer of the revenue cutter "McCulloch" at San Francisco, Cal., May 1, 1914, for duty in the summer cruise in Alaskan waters. April 17, 1914.

Waring, C. H., Acting Assistant Surgeon. Directed to proceed to Milledgeville, Ga., for duty in connection with epidemiological studies of pellagra under the direction of Surgeon Joseph Goldberger. April 22, 1914.

Taylor, H. A., Technical Assistant. Directed, upon receipt of instructions from Surgeon R. H. von Ezdorf, in charge of malaria investigations, to proceed from time to time to such places in the Southern States as he may designate for the purpose of making malaria surveys, collecting specimens, etc. April 23, 1914.

Willets, David G., Technical Assistant. Directed to proceed to Milledgeville, Ga., via Washington, D. C., for duty in connection with field investigations of pellagra. April 24, 1914.

Holt, E. M., Pharmacist. Directed to proceed to Fontainebleau, Miss., to superintend shipment of serviceable property to the New Orleans Quarantine Station, then to proceed to New Orleans Quarantine Station for temporary duty. April 27, 1914.

Smith, L. C., Pharmacist. Directed to accompany Passed Assistant Surgeon R. A. Herring to the Savannah Quarantine Station for the purpose of selecting such articles of furniture, shipped from Blackbeard Island, as will be useful in the special hospital to be established in Spartanburg, S. C. April 21, 1914.

BOARDS CONVENED.

Board of medical officers convened to meet at Portland, Me., for the re-examination of an alien certified for trachoma.

Detail for the Board:

Surgeon W. P. McIntosh, chairman.
Surgeon H. S. Mathewson, member.
Acting Assistant Surgeon A. F. Stuart, recorder. April 25, 1914.

Board of medical officers convened to meet at Buffalo, N. Y., for the re-examination of two aliens certified for trachoma.

Detail for the Board:

Surgeon C. H. Gardner, chairman.
Acting Assistant Surgeon W. L. Savage, member.
Acting Assistant Surgeon W. K. O'Callaghan, recorder. April 22, 1914.

Official: RUPERT BLUE,
Surgeon-General.

List of Changes of Stations and Duties of Commissioned and Other Officers of the United States Public Health Service for the Seven Days Ended May 6, 1914.

Carter, H. R., Senior Surgeon. Directed to proceed to the Bureau, Washington, D. C., April 28, 1914, for conference relative to quarantine matters. April 29, 1914.

Directed to proceed to Mobile, Ala., and such other places in the Southern States as may be necessary, to assume charge and direct malarial investigations. April 30, 1914.

Carmichael, D. A., Senior Surgeon. Granted 14 days' leave of absence from May 27, 1914. May 2, 1914.

Brooks, S. D., Senior Surgeon. Leave of absence for 6 days from April 18, 1914, amended to read "6 days' leave of absence from April 20, 1914." May 1, 1914.

Sprague, E. K., Surgeon. Detailed to attend the meeting of the American Association for Promoting Hygiene and Public Baths at Newark, N. J., May 13, 1914. May 2, 1914.

Granted 6 days' leave of absence from April 21, 1914, on account of sickness. May 2, 1914.

Schereschewsky, J. W., Surgeon. Detailed to represent the Service at the annual meeting of the National Association for the Study and Prevention of Tuberculosis, to be held at Washington, D. C., May 7-9, 1914. May 5, 1914.

Gwyn, M. K., Surgeon. Granted one month's leave of absence from April 14, 1914, on account of sickness. May 2, 1914.

Spratt, R. D., Passed Assistant Surgeon. Directed to proceed to Rochester, Pa., for the re-examination of an alien to observe results of a grattage operation. April 30, 1914.

Mullan, E. H., Passed Assistant Surgeon. Re-assigned to duty at the Immigration Station, Ellis Island, N. Y., effective May 20, 1914, in accordance with paragraph 168, Service Regulations. May 5, 1914.

Olesen, Robert, Passed Assistant Surgeon. Granted 7 days' leave of absence from April 26, 1914, on account of sickness. May 2, 1914.

Leake, J. P., Passed Assistant Surgeon. Directed to proceed via Eccles, W. Va., in company with the Director of the Bureau of Mines to investigate mine explosion at that place. On completion of this duty directed to proceed to Bowling Green and other places in Kentucky for investigations of smallpox. April 29, 1914.

Bailey, C. A., Acting Assistant Surgeon. Directed to proceed via Washington, D. C., to Quebec, Canada, for duty in the medical examination of immigrants. April 29, 1914.

Schug, F. J., Acting Assistant Surgeon. Directed to proceed to Seattle, Washington, for instruction by Surgeon B. J. Lloyd in the diagnosis of trachoma. April 30, 1914.

Roehrig, A. M., Pharmacist, re-assigned to duty at the Marine Hospital, Buffalo, N. Y., effective March 24, 1914, under paragraph 168, Service Regulations. May 5, 1914.

Scott, E. B., Pharmacist. Granted 1 day's leave of absence, May 5, 1914. May 2, 1914.

Official: RUPERT BLUE,
Surgeon-General.

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List of Changes of Stations and Duties of Commissioned and Other Officers of the United States Public Health Service for the Seven Days Ended May 13, 1914.

Assistant Surgeon General J. W. Trask. Detailed to attend the meeting of the National Conference of Charities and Corrections to be held in Memphis, Tenn., May 15, 1914, for the purpose of presenting a paper before the Public Health Section of the conference.

Also to stop *en route* at Bellbuckle, Tenn., for the purpose of delivering a public health address at the Training School for Boys in that town. May 8, 1914.

Senior Surgeon C. E. Banks. Granted 5 days' leave of absence, from May 15, 1914. May 6, 1914.

Surgeon W. J. Pettus. Granted 2 months' leave of absence, with pay, from May 21, 1914, and 3 months' leave of absence without pay, from July 21, 1914, with permission to go beyond the sea. May 11, 1914.

Surgeon C. P. Wertenbaker. Granted 1 month's leave of absence, on account of sickness, from May 10, 1914. May 9, 1914.

Surgeon M. H. Foster. Directed to proceed to Saratoga Springs, N. Y., to make a re-examination of an alien for the purpose of ascertaining the result of the grattage operation. May 11, 1914.

Surgeon C. W. Vogel. Granted 1 day's leave of absence, April 22, 1914, and 14 days' additional leave of absence, from April 29, 1914, on account of sickness. May 12, 1914.

Passed Assistant Surgeons A. M. Stimson, W. C. Rucker, Richard H. Creel, R. E. Ebersole, and J. W. Trask. Directed to report to the chairman of a board of commissioned medical officers at the Bureau, June 11, 1914, for examination to determine their fitness for promotion to the grade of Surgeon. May 11, 1914.

Passed Assistant Surgeon R. D. Spratt. Granted 4 days' leave of absence from May 16, 1914. May 6, 1914.

Passed Assistant Surgeon J. P. Leake. On request of the State Board of Health of Kentucky, directed to proceed to Bowling Green, Ky., and such other points in that State as may be necessary to make an investigation of smallpox and the relation of vaccine to its prevention. April 28, 1914.

Assistant Surgeons R. A. Kearny, W. F. Draper, and J. M. Gillespie. Directed to report to the Chairman of a board of commissioned medical officers at the Bureau, June 8, 1914, for examination to determine their fitness for promotion to the grade of Passed Assistant Surgeon. May 11, 1914.

Assistant Surgeon R. C. Derivaux. Directed to proceed to such points in the Southern States as the officer in charge of the malaria investigations may indicate for the purpose of making malaria surveys, collecting specimens, etc., May 8, 1914.

Assistant Surgeon J. S. Ruoff. Relieved from duty at the Marine Hospital, Stapleton, N. Y., and directed to proceed to the Sanatorium, Fort Stanton, N. M., and report to the medical officer in charge for duty and assignment to quarters. May 7, 1914.

Acting Assistant Surgeon R. E. Wynne. Directed to proceed to Martinsburg, W. Va., for duty in field investigations of the public health. May 9, 1914.

Technical Assistant H. A. Taylor. Directed to proceed to such points in the Southern States as the officer in charge of the malaria investigation may indicate for the purpose of making malaria surveys, collecting specimens, etc. May 9, 1914.

PROMOTION.

Assistant Surgeon Carlisle P. Knight promoted and commissioned as Passed Assistant Surgeon, effective March 25, 1914. April 29, 1914.

BOARDS CONVENED.

Board of commissioned medical officers convened to meet at the Bureau, June 8, 1914, for the purpose of examining certain Assistant Surgeons to determine their fitness for promotion to the grade of Passed Assistant Surgeon.

Also to convene at the Bureau, June 11, 1914, for the purpose of examining certain Passed Assistant Surgeons to determine their fitness for promotion to the grade of Surgeon.

Detail for the Board:

Assistant Surgeon-General W. G. Stimpson, Chairman.
Senior Surgeon H. W. Austin, Member.
Surgeon H. S. Cumming, Recorder. May 11, 1914.

Detail for board of commissioned medical officers convened for preparation of a new "Nomenclature of Diseases" amended as follows:

Assistant Surgeon-General W. C. Rucker, Chairman.
Assistant Surgeon-General J. W. Trask, Member.
Passed Assistant Surgeon Hugh de Valin, Recorder. May 11, 1914.

Board of medical officers convened to meet

at Detroit, Mich., for the re-examination of a detained alien.

Detail for the Board:

Senior Surgeon H. W. Austin, Chairman.
Assistant Surgeon J. H. Linson, Member.
Acting Assistant Surgeon K. L. Weber, Recorder. May 11, 1914.

Official: RUPERT BLUE,
Surgeon-General.

## Changes of Address

All changes of address of members should be sent to the General Secretary promptly.

The Association will not be responsible for non-delivery of the Annual Volume or Year Book, or of the JOURNAL unless notice of change of address is received before shipment or mailing.

Both the old and the new address should be given, thus:

HENRY MILTON,
From 2342 Albion Place, St. Louis, Mo.
To 278 Dartmouth St., Boston, Mass.

Titles or degrees to be used in publications or in the official records should be given, and names should be *plainly* written, or typewritten.

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BROWN, C. L.,
From Letterman Gen, Hosp., San Francisco, Cal.
To Attending Surgeon's Office, Soldiers' Home, Washington, D. C.

BERNARD, P. A.,
From 258 W. 74th St., New York, N. Y.
To G. P. O. Box 45, or 662 West End Ave., N. Y., N. Y.

BEHRE, JOHN R., Serg. 1st Cl.,
From Division Hospital, Manila, P. I.
To Department Hospital, Manila, P. I.

COUSSANS, BETTIE PRINCE,
From 5125 Morgan St., St. Louis, Mo.
To Sherman Hospital, Sherman, Texas.

DIETZ, H. W.,
From Augur Barracks, Jolo, P. I.
To Field Hosp. No. 4, Ft. Wm. McKinley, Rizal, P. I.

DAHL, FRED,
From 148 Parker St., Newark, N. J.
To 52 Shepard Ave., East Orange, N. J.

FEIN, MARY AUGUSTINE,
From 1114 Thayer Ave., Little Rock, Ark.
To Little Rock, Ark.

GEDDES, MRS. L. M.,
From 393 Cambridge St., Allston, Boston, Mass.
To 1377a Commonwealth Ave., Allston, Boston, Mass.

GENOCHIO, EDW. P.,
From care Medical College, Ft. Worth, Tex.
To 1709 Jackson Blvd., Apt. K, Chicago, Ill.

HOEY, CHAS. E.,
From 11 Frederick St., S. Framingham, Mass.
To 459 Dudley St., Roxbury, Mass.

HOLT, FRANK,
From Post Hosp., Torrey Barracks, P. I.
To Camp John Hay, P. I.

LEE, J. V.,
From 829 Davis St., Evanston, Ill.
To N. E. cor. Main St. and Chicago Ave. Evanston, Ill.

MALLARD, A. E.,
From 32 Adams Ave., N., Detroit, Mich.
To 287 Woodward Ave., Detroit, Mich.

OSBORNE, WM., JR.,
From Danforth, Mo.
To Presque Isle, Me., P. O. Box 304.

PARKER, G. R.,
From 227 Plainfield St., Providence, R. I.
To 22 Pocasset Ave., Providence, R. I.

PAUL, GEO.,
From Ft. Mills, Corregidor, P. I.
To 226 Superior St., Salem, Ore.

PIERSON, ROMAINE,
From 108 Fulton St., New York, N. Y.
To 81-83 Fulton St., New York, N. Y.

WALL, O. A.,
From 4332 Virginia Ave., St. Louis, Mo.
To 4106 W. Pine St., St. Louis, Mo.

WHITNEY, DAVID,
From 4342 Campbell St., Kansas City, Mo.
To 714 Wyandotte St., Kansas City, Mo.

## THE OLD AND THE NEW.

Because something recently introduced may prove highly useful, we must not jump to the conclusion that it should supersede everything long similarily used with great success. Though the trend of modern progress is ever forward, we are often forced to realize that some of our best recent achievements do not equal some of the triumphs of an earlier period. Notably is that true in the field of art, though illustrations are not lacking elsewhere. The ablest sculptors of our day have not equaled the sublime creations of their illustrious colleagues among the ancient Greeks and the Italians of the sixteenth century. No painter of our time has given us anything quite comparable with the masterpieces of Raphael and Correggio, of Titian and Rembrandt, Jacob Ruysdael, Holbein, Velasquez, and many others. Though the modern piano has utterly eclipsed the old-time spinet and harpsichord, and though, in technique and tone, the world has not seen the equal of such men as Liszt and Rubenstein, Paderewski and Mark Hamburg, no living composer has written anything which classes with the great works of Beethoven, of Mozart, Schumann and Chopin, while in the field of the musical drama the world is still waiting for the worthy successor of Wagner; and while the piano and its great exponents have scored such signal triumphs, no contemporary violin maker has equaled a Stradivarius or an Amati, and no wizard of the bow, now before the public, will claim to be the rival of Paganini. The modern express train and the giant ocean liner are immeasurably ahead of the stage coach of our ancestors and the galley of the ancients. The high powered automobile has utterly outstripped the horse, and can easily distance the stoutest thoroughbred, yet there are no indications that the noble animal will be permitted to become extinct or to revert to the type of his diminutive prehistoric ancestor; and tnough by reason of certain very narrow and ill-advised legislation, notably in our Empire State, the thoroughbred has suffered a sad diminution in value, in England and some other countries where broader and more enlightened ideas and cleaner politics have prevailed he is held in universal admiration, and the sport of kings still flourishes as of yore.

The foregoing random illustrations should remind us that, while we do well to remain alert and watchful for substantial improvements, we should hold on with a firm and unrelaxing grasp to everything which long experience has proved to be good.—*R. Ottolengui, M. D. S., LL. D., D. D. S., in Lehn & Fink's Dentist's Diary.*

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## THE ADVANTAGE OF DISCOUNTING BILLS.

It is the part of good business policy to make every effort to discount bills. Money can be used in no better way. From 2 to 10 percent is offered on ten-day discounts on drug, merchandise, cigar, gas and other bills. This is well worth picking up. It is almost like finding money. Almost anything else may be properly neglected to conserve the money for discounting bills. Aside from the money saved, it gives you a standing with the wholesalers and jobbers that nothing else will. Such standing is a valuable asset in the business world, and one that every business man should strive to gain. It means larger opportunities and will be a strong help in times of financial trouble.—W. S. Adkins in *The National Druggist.*